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A.M.A. ARCHIVES OF

DERMATOLOGY

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The New, Newer, and Newest

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*Ref.: Aaron, J. N. "The Use of Hydeltra T.B.A. in Hypertrophic Lichen Planus Utilizing the Vibra-Puncture Technique" Arch. of Dermatology, November 1958

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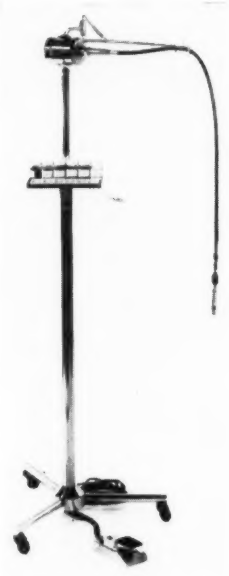

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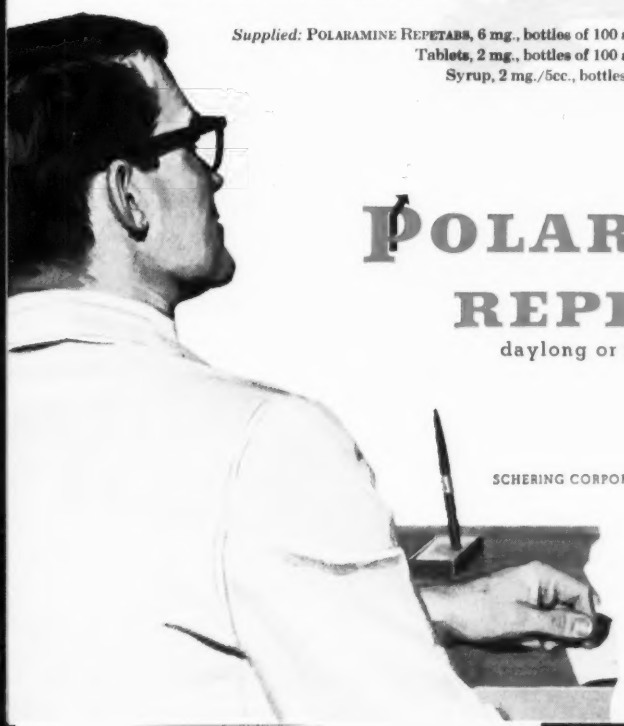

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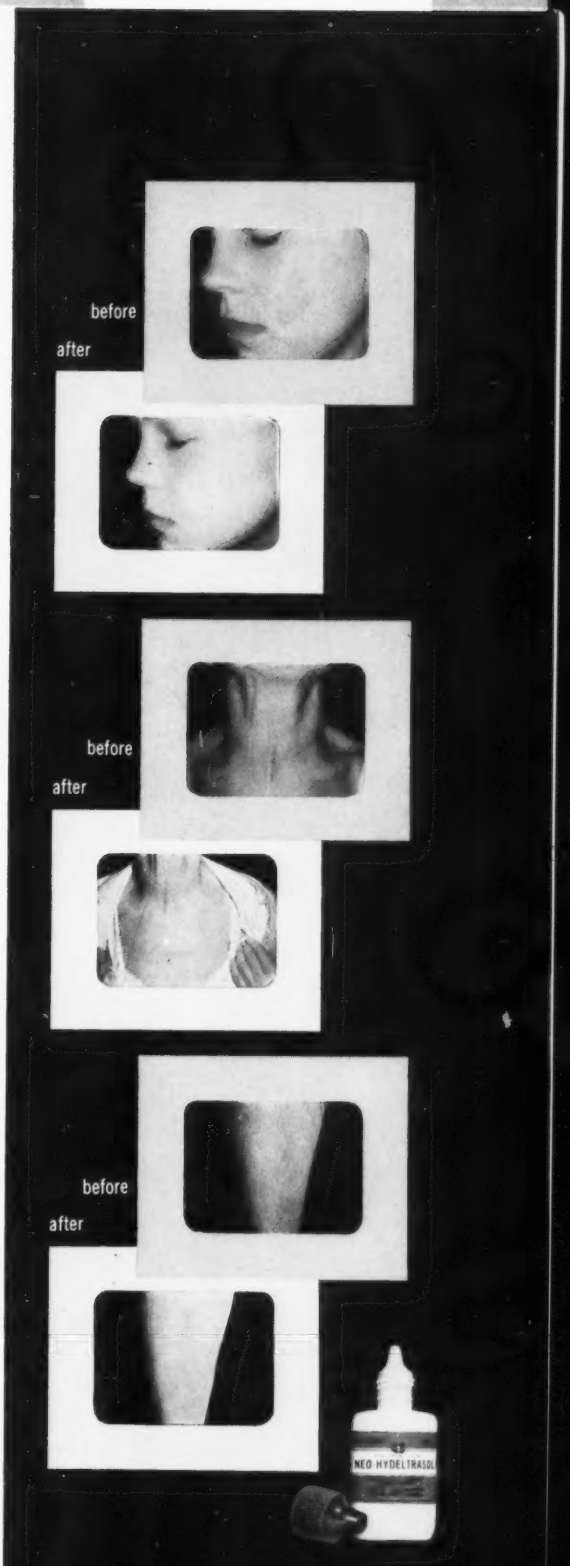

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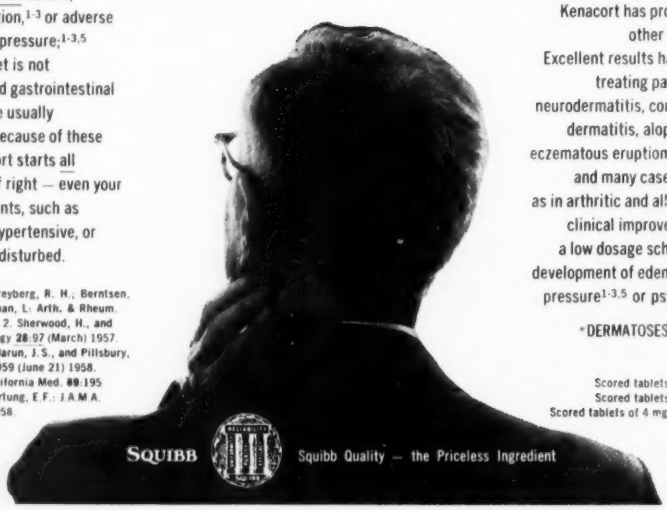

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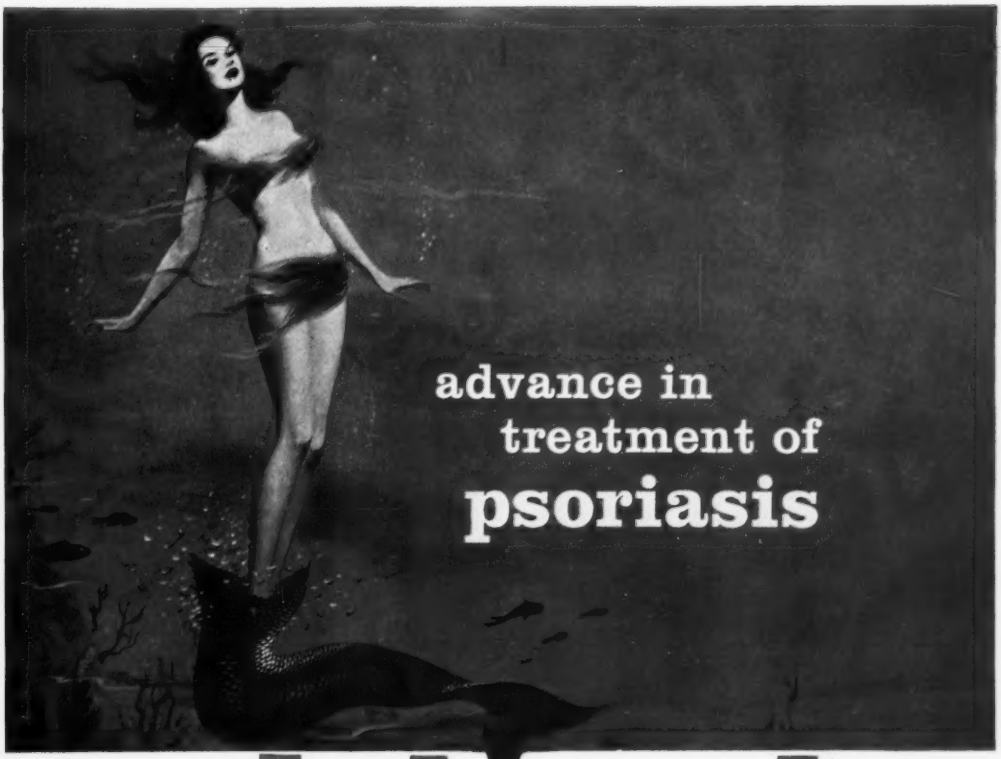

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AVEENO OINTMENT is now available in a 4 oz. economy size tube as well as the 1 oz. tube.

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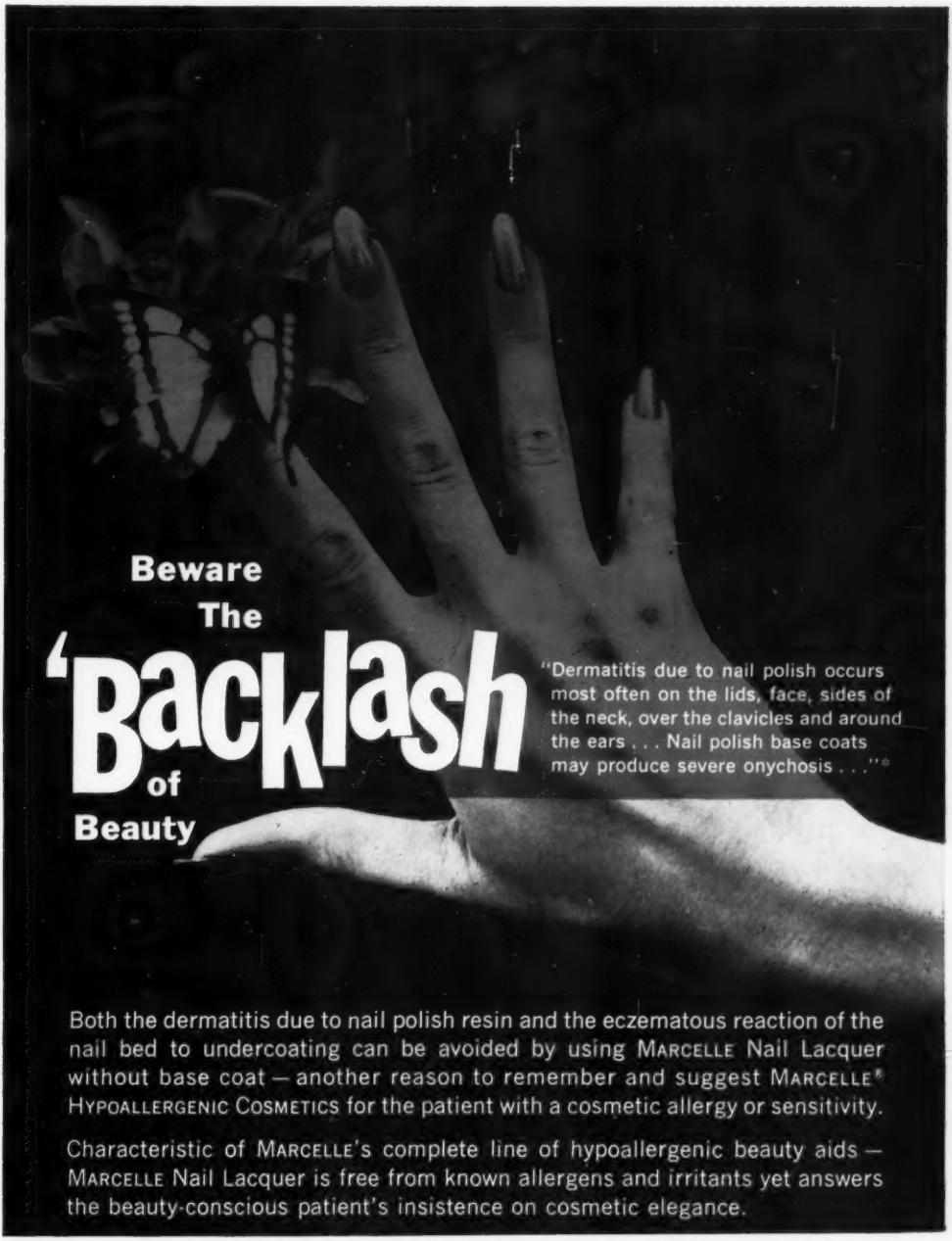
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"Dermatitis due to nail polish occurs most often on the lids, face, sides of the neck, over the clavicles and around the ears . . . Nail polish base coats may produce severe onychosis . . ."*
Both the dermatitis due to nail polish resin and the eczematous reaction of the nail bed to undercoating can be avoided by using MARCELLE Nail Lacquer without base coat — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.
Characteristic of MARCELLE's complete line of hypoallergenic beauty aids — MARCELLE Nail Lacquer is free from known allergens and irritants yet answers the beauty-conscious patient's insistence on cosmetic elegance.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Andrews, G. C.: Diseases of the Skin, ed. 4, Philadelphia, Saunders, 1954, pp. 117, 118

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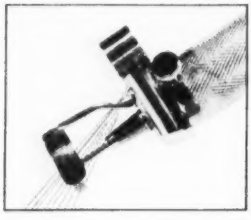
(100% dichloro-tetrafluoro-ethane...contains no ethyl-chloride)

SKIN REFRIGERANT–ANESTHETIC

*Widely Accepted for Local Anesthesia in Surgical Planing of the Skin**

JET-SPRAY PLANER

This hand-tooled, precision-built instrument with diamond fraises is available for most standard planing units. In ordering, please specify make of planing unit. Full information on request.



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**A.M.A. Archives of Dermatology, April 1955*
Ref.: Wilson, J. W.; Luikart II, R.; Ayres III, S., Reprints available

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coal tar therapy with cosmetic consideration

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This pleasant English coal tar solution is a time-proven dermatologic standard of reliability on two continents. In elegance, it is superior to the usual crude coal tar preparations.

Whether you prescribe WRIGHT'S L.C.D. for application in its undiluted form or by incorporation in ointments and lotions, your patient will be pleased with its ease of applicability and removal, the absence of greasy staining.

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Indicated in chronic psoriasis, atopic dermatitis, chronic eczematous disorders and many other dermatoses.

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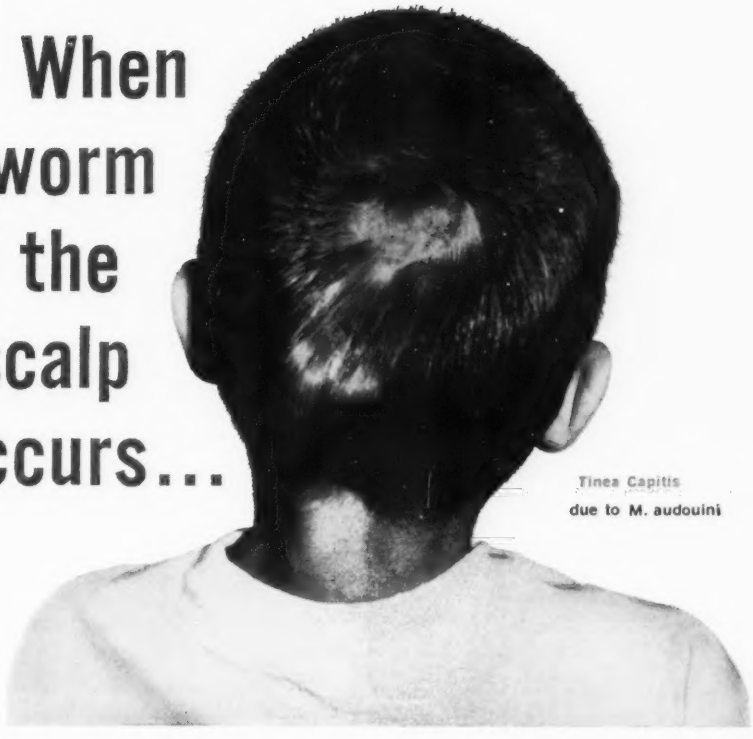
FOUGERA **Hicksville, Long Island, New York**

When ringworm of the scalp occurs...



Tinea Capitis
due to M. audouini

. . . topical antifungal therapy is recommended as immediate treatment. Prompt use of Salundek will destroy accessible spores and form a protective coating, reducing the likelihood of spread of the disease to other areas of the scalp, or to other children.

*New Dosage Form, Salundek Solution** – It is supplied in 3-ounce bottles with a controlled flow applicator cap. Now there is a choice that will lead to better patient cooperation during the treatment of this stubborn disease.

Many investigators have reported that the ointment and the solution have the same high percentage of cures, obtained in an average of 12 to 16 weeks.

Salundek also eliminates the hazard of x-ray therapy • seldom causes skin reaction • offers convenience in use – no stain, no odor and no effect on future hair growth.

Supplied: SALUNDEK OINTMENT, 2 oz. tubes and 1 lb. jars. SALUNDEK SOLUTION, 3 oz. bottles with controlled flow applicator cap.

Write for supply of "Instructions for Home Care" pads.

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(Brand of Zinchlorundesal)

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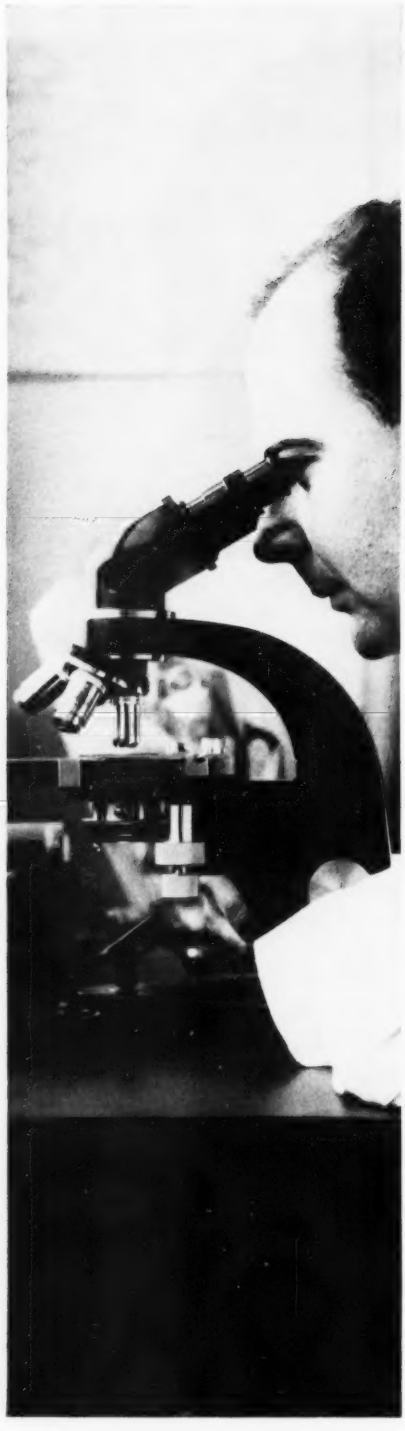
*In the presence of open lesions, the use of the ointment may be preferred at first since the base of the solution causes occasional transient stinging. Avoid contact with the eyes.



COSMETOLOGY

...and what it means to your patients

Cosmetics and the Modern Woman

Now more than ever, cosmetics exert major influences in the life of the modern woman—your patient. The right preparations provide real psychological benefits. To be conscious of looking better is to feel better. Carefully selected and skillfully applied cosmetics complement her dress and accessories. They may prove invaluable in the achievement of a successful business career or for increased social recognition. And for her outdoor activities, creams and lotions protect against excess drying, chapping and scaling from overexposure to low humidities, the hot sun and temperature extremes.

Applied Science to Cosmetic Art

Strides have been made in recent years toward greatly improved cosmetic products through scientific formulation and precise quality control. Recent discoveries and technologic methods from the chemical and physical sciences as well as from dermatologic research have contributed to this progress. And there are new research vistas about to appear because "The need for increasing the scope and number of investigations relating to fundamental problems of skin physiology, biochemistry, pharmacology, and toxicology cannot be stressed too strongly."[1]

Beauty Through Cosmetology

The Helena Rubinstein Laboratories has devoted thirty-five years to studying cosmetics, skin structure and function. This group has contributed to the development of new compounds and synthetics—the complex aromatics, the emulsifiers, the emollients, the catalysts—and how they may best be utilized for improved cosmetology.

1. Lehman, A. J.: J.A.M.A. *164*:416 (May 25) 1957.

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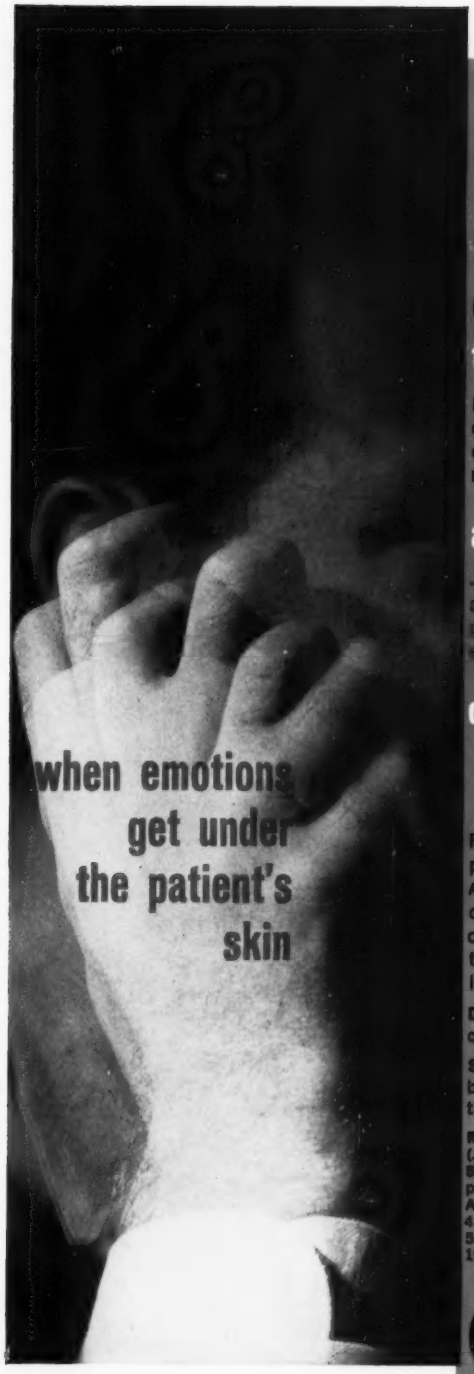

A TRANQUILIZER UNIQUE
IN DERMATOLOGIC PRACTICE

dermatoses respond to the calming action

Feinberg: "Tranquilizing drugs in general have an equivocal effect on the manifestations of allergic disease. . . . ATARAX may be one exception to the rule. . . ."[1]

and the anti-allergic effect

—Added antihistaminic action of ATARAX controls a wide variety of dermatological exacerbations: pruritus, urticaria, dermatitis, and other cutaneous eruptions.[2,3,4,5]

of ATARAX®

(brand of hydroxyzine)

Feinberg[1] obtained "most striking results" in 17 patients with chronic urticaria. The effect of ATARAX was excellent in 15, fair to good in 2. After objective evaluation of 140 patients, Robinson[2] concludes that ATARAX is "valuable adjunctive therapy" for patients whose dermatoses are related to emotional tension.

Dosage: Adults, one 25 mg. tablet, or one tbsp. Syrup q.i.d. Children, 1 or 2 tsp. Syrup t.i.d.

Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Feinberg, A. R., et al.: J. Allergy 29:358 (July) 1958. 2. Robinson, H. M., Jr., et al.: South. M. J. 50:1282 (Oct.) 1957. 3. Santos, I. M., and Unger, L.: Paper presented at 14th Annual Congress, American College of Allergists, Atlantic City, New Jersey, April 23-25, 1958. 4. Coirault, M., et al.: Presse méd. 64:2239 (Dec. 26) 1956. 5. Robinson, H. J., Jr., et al.: J.A.M.A. 161:604 (June 16) 1956.

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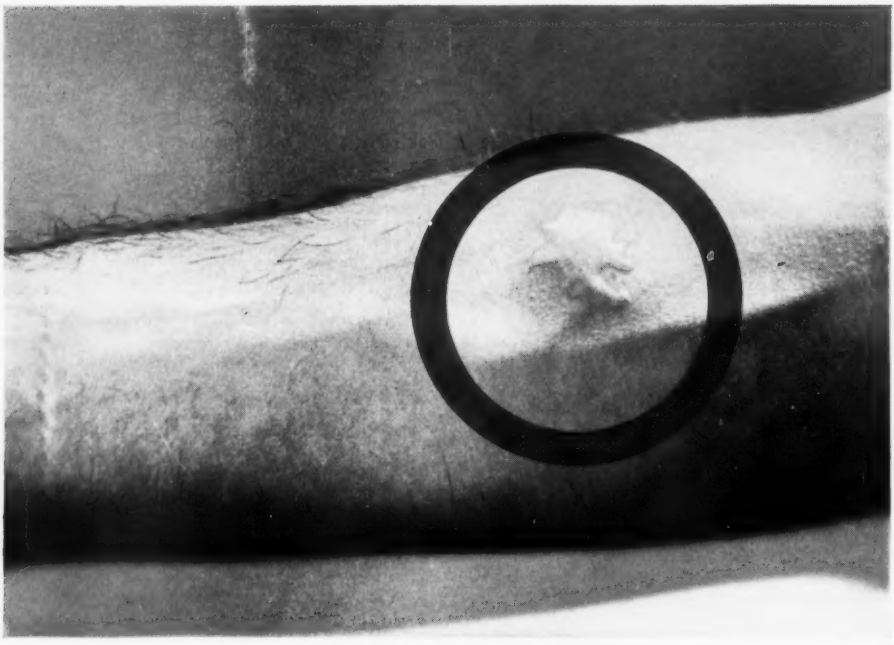
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

all-day (and all-night) relief from histamine-caused skin reactions . . .



The vast majority of your patients who suffer from histamine-caused skin reactions get all-day and all-night relief with just one 'Teldrin' *Spansule* capsule q12h. Relief is rapid as well as prolonged, since one third of the 'Teldrin' medication is released within minutes, the rest over a period of 8 to 10 hours. And side effects are minimal.

Available: 8 mg. (for younger children) and 12 mg. 'Teldrin' *Spansule* capsules.

TELDRIN® brand of chlorprophenpyridamine maleate

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TO PROTECT SKIN

AGAINST A WIDE RANGE OF IRRITANTS

- *in industry*
- *in the home*

Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

SUGGESTED DOSAGE: Cleanse area thoroughly with soap and water. Apply thin film as required and rub in well. If skin is exposed constantly to irritant, apply every 2-4 hours, or as needed to provide protection. It is not necessary to remove original coat before applying subsequent coats. Any objectionable greasiness may be removed by wiping with a dry cloth, or washing gently with soap and water.

CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
Industrial Dermatoses
Chapping—Chafing
Intertrigo
Diaper Rash
Chronic Dermatoses
Aggravated by Soap and Water

SILICOTE CONTAINS
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble inactive ents.

Send for samples and literature

1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

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SILICONE OINTMENT

ARNAR-STONE LABORATORIES, INC. MT. PROSPECT, ILLINOIS

In Canada: Brent Laboratories, Ltd., Toronto

HIGHLIGHTS FROM THE A.M.A. COUNCIL ON DRUGS

REPORT ON TRIAMCINOLONE

J.A.M.A. 169:257 (January 17) 1959.

"It [triamcinolone] has an anti-inflammatory potency greater than an equal amount of prednisolone; i.e., comparable suppressive effects may usually be achieved with lower doses of triamcinolone than with prednisolone."

"Triamcinolone lacks the sodium-retaining and edema-producing effects of most other glucocorticoids. During the first several days of administration, it may cause a loss of sodium from the body; an initial mild diuretic action is frequently observed, whether the patient is frankly edematous or not. This is in contrast to the definite sodium-retaining and fluid-retaining properties of cortisone and hydrocortisone and to a much lesser extent with prednisone and prednisolone."

"Except in exceedingly large doses, triamcinolone apparently has no consistent effect on potassium excretion. Hence, neither sodium restriction nor potassium supplementation is ordinarily required during therapy with this agent."

"As with other glucocorticoids, the long-term administration of triamcinolone results in definite catabolic effects, as indicated by impairment of carbohydrate utilization and negative protein and calcium balance. This catabolic effect, coupled with a lack of appetite stimulation which is apparently peculiar to triamcinolone, may produce weight loss that might be undesirable in some patients treated for long periods of time."

"...the voracious appetite, with weight gain and euphoria, characteristic of other steroids, is not seen with administration of triamcinolone."

"Triamcinolone has been used for the management of a wide variety of clinical conditions usually considered amenable to systemic steroid therapy. These have included rheumatoid arthritis and other collagen diseases, allergic and dermatological disorders, certain leukemias and malignant lymphomas, the nephrotic syndrome, pulmonary emphysema and fibrosis, acute bursitis, rheumatic fever, and certain blood dyscrasias. Although clinical experience with the drug in some of the foregoing conditions is not extensive, the many similarities in action between triamcinolone and other potent glucocorticoids would indicate a usefulness for triamcinolone akin to that of other agents of this class."

"There is some evidence that triamcinolone is more effective at a smaller dosage than are other steroids in controlling both the skin and joint lesions in psoriasis, whether or not complicated by arthropathy."

"Triamcinolone appears to compare favorably with other steroids for use in those situations in which edema and sodium retention have been complicating problems."

"It [triamcinolone] may also be the steroid of choice for patients in whom psychic stimulation, euphoria, voracious appetite, and weight gain should be avoided."

"...the drug [triamcinolone] does produce the other side effects and untoward reactions common to the glucocorticoids. At therapeutically equivalent doses, the frequency and severity of clinical manifestations of hyperadrenalism — rounding of the face, fat deposition, and hirsutism — are essentially the same. Likewise, there is little indication that the relative incidence of osteoporosis is materially decreased after the long-term use of the drug."

"Triamcinolone apparently does not cause the euphoria sometimes seen with other steroids, and the occurrence of mental depressions is uncommon."

"Current evidence suggests that the drug [triamcinolone] may not produce as high an incidence of peptic ulcer as do other steroids."

"Cutaneous erythema seems to be a side effect peculiar to triamcinolone."

"The usual contraindications and precautions of glucocorticoid therapy should be followed in the use of triamcinolone, keeping in mind that prolonged therapy with this drug will suppress the function of the patient's own adrenals by interfering with the pituitary-adrenal axis."

Aristocort®

Triamcinolone LEDERLE

Supplied: 1 mg. scored tablets (yellow)
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LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

A NEW WIDE-SPECTRUM TOPICAL MICROBICIDE

not an antibiotic... not a sulfonamide... not a nitrofuran

Triburon

CHLORIDE

& Triburon-HC

(containing hydrocortisone 0.5%)

EFFECTIVE EVEN AGAINST ANTIBIOTIC-RESISTANT STRAINS

HIGHLY ACTIVE

■ against most "pathogenic cocci [both staphylococci and streptococci] regardless of their resistance to antibiotics."[1]

■ against pathogens common in skin and wound infections.

VIRTUALLY NONSENSITIZING

■ in more than 4500 stringent, closed-patch sensitivity tests, the incidence of allergic response was less than 2 per cent.[2, 3]

■ in initial clinical studies, only 15 of 1014 patients developed evidence of skin irritation.

MINIMAL RESISTANT ORGANISMS

■ laboratory attempts to develop Triburon-resistant strains produced no substantial change in organism sensitivity.[1]

■ WIDE-SPECTRUM
■ RAPID-ACTING
■ WELL TOLERATED
■ NONSTAINING
■ ODORLESS

DIAGNOSIS AND NO. OF PATIENTS	DURATION OF TREATMENT	RESULTS	ADVERSE REACTIONS
Impetigo contagiosa (50)	Triburon 3-10 days	excellent	none
Ecthyma (24)	Triburon 5-14 days	excellent	none
Pustular folliculitis (16)	Triburon 1-3 weeks	infection controlled	3 complaints of burning
Dermatitis repens (18)	Triburon 1-2 weeks	infection controlled	none
Dermatitis repens (18)	Triburon-HC 1-4 weeks	excellent	none
Secondarily infected eczematous eruption (20)	Triburon 1-2 weeks	infection controlled	none
Secondarily infected eczematous eruption (64)	Triburon-HC 1-4 weeks	excellent	1 complaint of irritation

Chart based on finding of E. Edelson, E. Grunberg and T. V. Morton Jr.

PACKAGES:
Triburon Ointment, 1-oz tubes and 1-lb jars.
Triburon-HC Ointment, 5-Gm and 20-Gm tubes.

REFERENCES: 1. R. J. Schnitzer, E. Grunberg, W. F. DeLorenzo and R. E. Bagdon, to be published.
2. E. Edelson, E. Grunberg and T. V. Morton, Jr., **Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959.**
3. R. C. V. Robinson and L. E. Harmon, **Antibiotics Annual 1958-1959.**

TRIBURON™- triclobisonium chloride — N,N'-bis[1-methyl-3-(2,2,6-trimethylcyclohexyl) propyl]-N,-N'-dimethyl-1,6-hexanediamine bis (methochloride). ROCHE®

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Never before in **ACNE!**

Graded long-term abrasion

The 3 grades of BRĀSIVOL permit a logical 3-step course of therapy:

1

Mild abrasion for 2-4 weeks with BRĀSIVOL FINE

2

More vigorous abrasion for 2-4 weeks with BRĀSIVOL MEDIUM

3

Maintenance treatment for as long as needed with BRĀSIVOL ROUGH

BRASIVOL introduces a new concept in the treatment of acne: prolonged superficial abrasion precisely adjustable to the patient's progress. Ten years of clinical studies in over a thousand acne patients have demonstrated the success of continuous abrasion in maintaining patency of the sebaceous ducts by gentle desquamation, thereby reducing comedones, papules, pustules and cysts, and minimizing post-acne scarring.

BRASIVOL contains non-silicon abrasives (fused synthetic aluminum oxide) of carefully selected particle sizes and in appropriate ratios, with hexachlorophene 1.0%, in a specially formulated base of soap and synthetic detergent.

1. Saperstein, R. B.: Presented at 107th annual meeting of American Medical Assn., San Francisco, Calif., June 23-27, 1958.

SUPPLIED:
Jars of Brāsivol Fine 6 oz.; Brāsivol Medium 6½ oz.; Brāsivol Rough 7 oz.

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three-way comparative study demonstrates "full-healing effect" of HYDRO-TAR™ in acute & chronic dermatoses

(Liquor Carbonis Detergens with Hydrocortisone, Almay)

A CASE IN POINT—ATOPIC DERMATITIS OF BOTH HANDS

1. Hydrocortisone alone suppresses inflammation. 2. Coal tar alone corrects eczematous manifestations. 3. Both agents combined in HYDRO-TAR speed complete early healing. Mutually supportive action produces the "full-healing" effect. Presence of hydrocortisone permits well-tolerated coal-tar therapy even during the acute phases of severe dermatoses.

Dosage: Apply by gentle massage to affected areas 3 or 4 times a day; 0.5% for moderately severe dermatoses or maintenance – 1.0% for severe dermatoses.

Supplied: 15 Gm. tubes in 0.5% and 1.0% strengths. Samples and literature sent on request.

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for dramatic relief of penicillin reactions—
early treatment with

NEUTRAPEN®

(NEUTRALIZES PENICILLIN) (Penicillinase Injectable,* SchenLabs)

the only specific for penicillin reactions

"Penicillinase [Neutrapen] should be given as soon as possible after onset of symptoms."[5]
(M. C. Zimmerman – Antibiotics Annual, 1957-58)

- effective in 97% of cases[1]
- acts within an hour, lasts up to a week[2,3]
- one injection sufficient in 80% of cases[1]
- itching abates promptly[4]
- most reactions clear in 12 to 96 hours[1,5]
- well tolerated[1-9]
- may be lifesaving in certain anaphylactoid reactions[6,7]

Obscure sources – even cases with no history of penicillin therapy respond to NEUTRAPEN if the reaction has been caused by penicillin from sources such as milk, Roquefort or Bleu cheese, or penicillin-containing vaccines.[1,5,9]

NEUTRAPEN – 800,000 units I. M. – should be given as soon as symptoms appear. May be repeated on the third day if response is not satisfactory. In anaphylactic reactions, epinephrine should be given and other supportive measures should be instituted immediately, followed by 800,000 units of NEUTRAPEN I. V. and 800,000 units I. M.

contraindications: None. *side effects:* Occasionally transient local soreness, erythema, and edema; rarely, transitory chills and fever. *supplied:* 800,000-unit, single-dose vials of lyophilized penicillinase powder. Stable at room temperature in the dry state.

References: (1) Zimmerman, M. C.: Clin. Med. *5*:305, 1958. (2) Becker, R. M.: New England J. Med. *254*:952, 1956. (3) Chen, J. Y. P.; Bard, J. W., and Balsito, A. A., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 321. (4) Minno, A. M., and Davis, G. M.: J.A.M.A. *165*:222 (Sept. 21), 1957. (5) Zimmerman, M. C., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 312. (6) Becker, R. M.: Ann. Int. Med. *48*:1228, 1958. (7) Becker, R. M., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 310. (8) Davis, G. M.: Discussion, Antibiotics Symposium, Washington, D. C., October 3, 1957. (9) Zimmerman, M. C.: J.A.M.A. *167*:1807 (Aug. 9), 1958.

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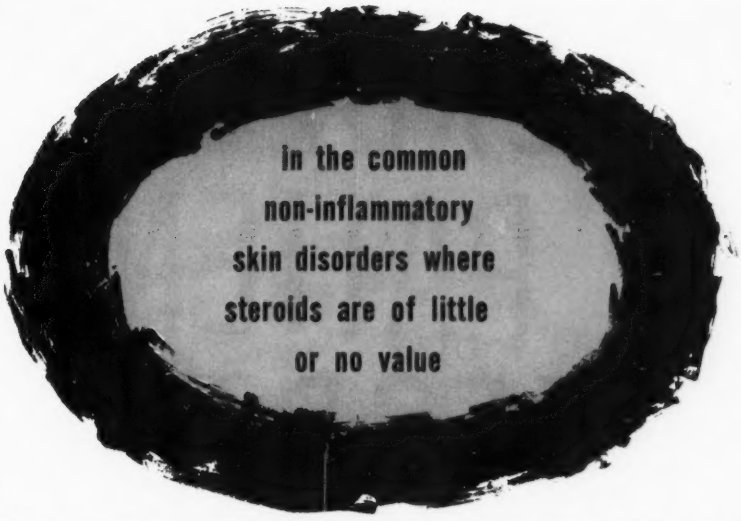

PRAGMATAR*

An outstanding tar-sulfur-salicylic acid ointment

SEBORRHEIC AFFECTIONS

including "cradle cap" and dandruff

FUNGOUS INFECTIONS

including "athlete's foot," tinea capitis, etc.

SUBACUTE AND CHRONIC DERMATITIS

where scaling and lichenification may be a problem

ECZEMATOUS ERUPTIONS

following acute dermatoses of various etiologies

Despite the advent of topical steroids, dermatologists continually reaffirm the value of the ingredients of 'Pragmatar'. Tar, sulfur and salicylic acid remain prominent, perhaps dominant, in the management of many non-inflammatory skin disturbances.

'Pragmatar'
- exerts a prompt yet gentle keratolytic-bacteriostatic effect.
- stimulates epithelization.
- relieves itching and burning.
- holds costs down for the patient when prolonged treatment is indicated.

And 'Pragmatar', a fundamental remedy in dermatologic practice since 1943, combines its ingredients in an outstanding vehicle. 'Pragmatar' is easy to apply and remove. It does not stain. It is completely free of the "skin-preparation odor" that many patients find embarrassing. Its wide margin of safety in both adults and children is well established.

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an unsurpassed topical anesthetic

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DYCLONE is a well tolerated topical anesthetic which is

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help restore emotional & mental balance with Covermark

Covermark conceals dermatological blemishes

Doctor, you are no doubt aware of the problems confronting patients with facial disfigurements. They are often subject to psychic, as well as social problems. When treating these patients, you will find COVERMARK to be of intrinsic value in your therapy.

WATERPROOF COVERMARK is a product which conceals skin discolorations, whether permanent or temporary. It is a neutral, opaque, hypo-allergenic cream which is waterproof and will not crack or flake.

COVERMARK can be used to conceal nevi such as vitiligo, post-operative scars, papules or pustules, varicose veins and other types of skin discolorations.

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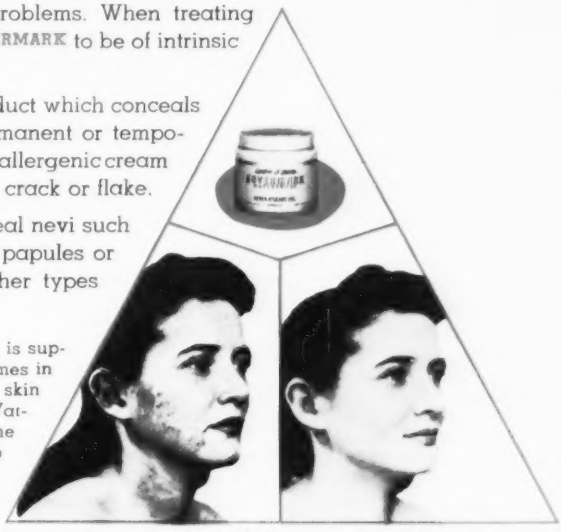

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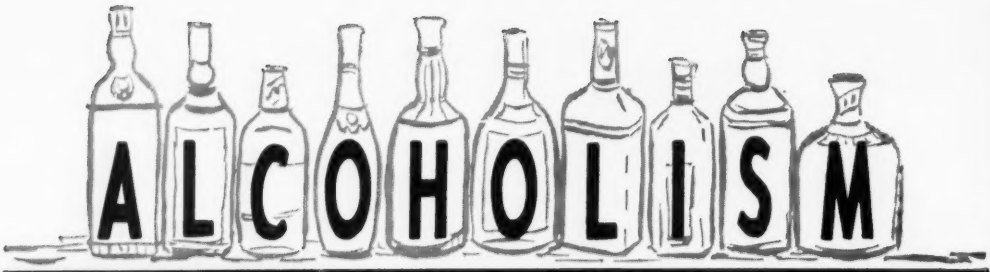

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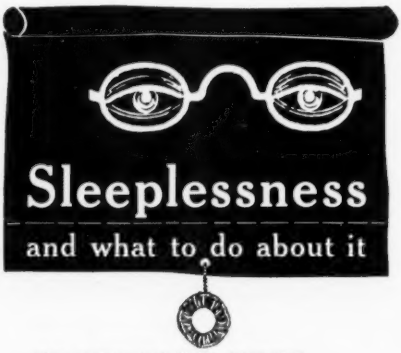

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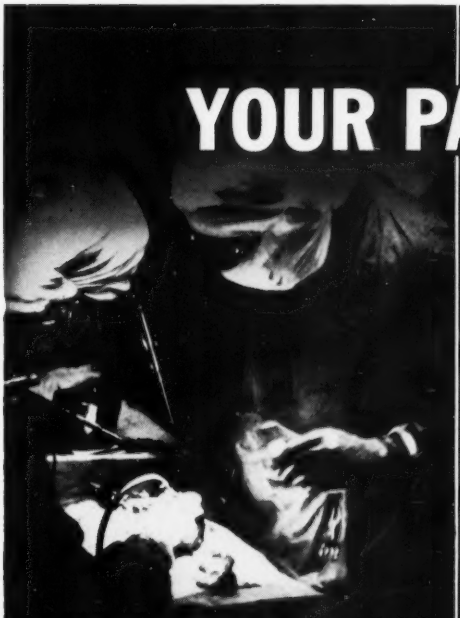

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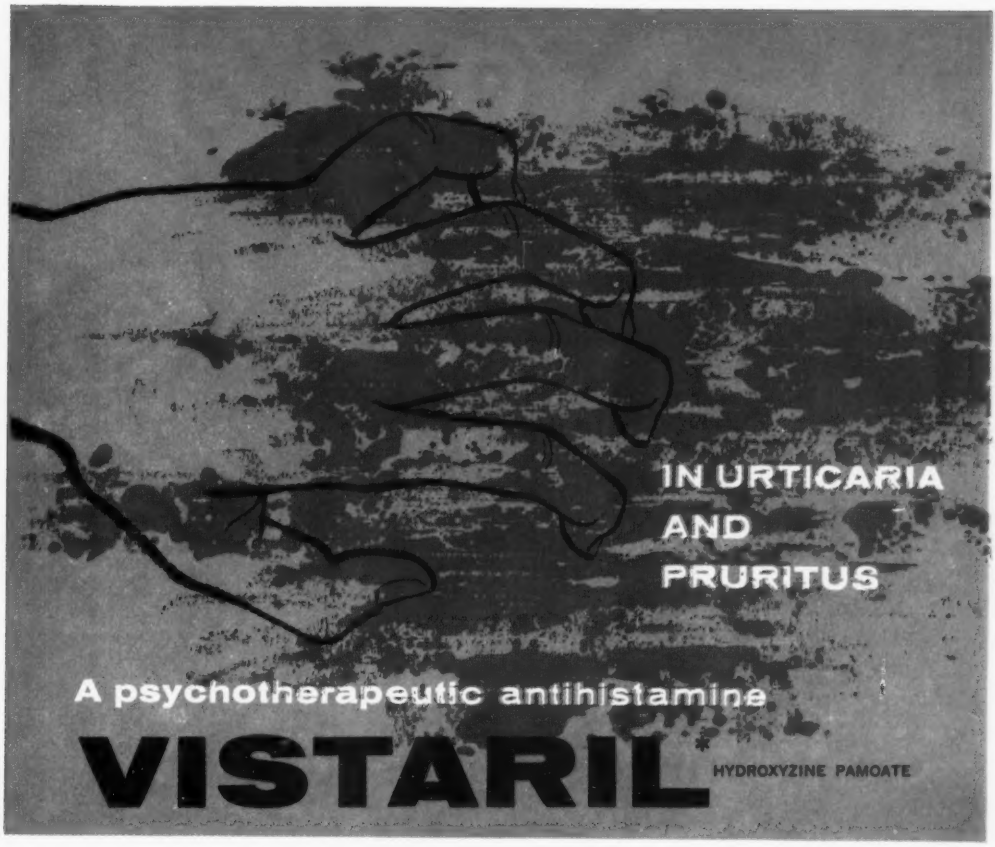

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Serotonin

Its Effect in Normal and Atopic Skin

W. E. CLENDENNING, M.D.; G. A. DeOREO, M.D., and R. B. STOUGHTON, M.D., Cleveland

Introduction

The purpose of this article is twofold: first, to summarize briefly those important aspects of serotonin metabolism which may interest the dermatologist; second, to present some observations we have made on the differences in response to intradermal injection of serotonin in the skin of normal adults as compared to the skin of people with atopic dermatitis.

As long ago as 1914, Masson presented the idea that cells in the wall of the intestines, which he termed argentaffin cells, might belong to an endocrine system similar to the chromaffin tissue of the adrenal medulla but differing in that the argentaffin cells are dispersed and do not form one organ.[1] This was perhaps the starting point of knowledge concerning the substance we now term serotonin (5-hydroxytryptamine, 5-HT, HT, 5-HTA, and Enteramine).

It was not until 1948 that this physiologically active agent was successfully isolated by Rapport, Green, and Page.[2] A measure of the phenomenal amount of interest in and work done on serotonin during the past decade is perhaps best illustrated in a recent review by Page,[3] which lists a bibliography of over 500 articles, all of which have appeared within the past four years.

Only a small number of these articles include any reference to the skin or its appendages. Of those which do, most have presented work which was done on the skin of lower animals, in particular the rat.[4-7] It now appears unlikely that work done with this substance on the skin of animals other than man will have much carry-over value, as it has been shown that human skin has very little measurable serotonin.[8]

Serotonin has been found in all of the phyla except the coelenterates. It has been suggested by Collier[9] that this widespread distribution indicates one of two things: Either the capacity to produce this substance is easily developed as occasion demands or the ability of production is primitive in evolution.

Serotonin is widespread in its distribution within the human body. Large amounts have been found in the gastrointestinal tract, the platelets, the spleen, and the brain. There are much smaller concentrations in liver and bone marrow and even less in the lung, thyroid, pancreas, and diaphragm. It has not been detected in skeletal muscle, in the peripheral nerves, or in the adrenal gland.[3,9]

Various workers have searched for serotonin in human skin. Some have failed to find even a trace, while others have detected minute amounts (0.01 mg. per gram). These

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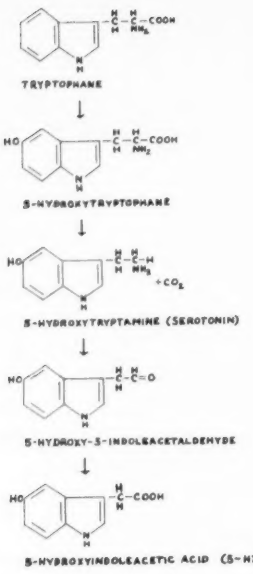
Resident in Dermatology, University Hospitals of Cleveland (Dr. Clendenning); Assistant Clinical Professor of Dermatology (Dr. DeOreo), and Director of Dermatology Western Reserve University (Dr. Stoughton).



amounts are so small that several observers have reached the conclusion that a physiologically active role for serotonin in the human integument is unlikely.[8,10-12] Of course, the existence of serotonin in a bound form, undetectable by present methods of determination, has not been conclusively ruled out.

Metabolism of Serotonin

Owing to the efforts of a number of workers, the metabolic pathways for the production and excretion of serotonin now seem fairly well established[3,13,14] (Diagram). The amino acid, tryptophan, is the major precursor of serotonin. Normally only about 1% of the dietary tryptophan is utilized for its formation. However, in patients with malignant carcinoid, as much as 60% of the dietary intake may be taken for this purpose. It has been suggested that this marked alteration in tryptophan metabolism may account for the pellagra-like symptoms noted in a small percentage of patients with this disorder.[3,15-17]

The first step in the conversion of tryptophan to serotonin is the addition of a hydroxyl group to the 5 position of tryptophan, to form a new amino acid, 5-hydroxytryptophan. The second step is the loss of CO_2 from the amino acid to form serotonin (5-hydroxytryptamine). This reaction is catalyzed by the enzyme 5-hydroxytrytophan decarboxylase, which is widely distributed throughout the body.

The inactivation of serotonin occurs by the process of oxidative deamination by the enzyme amine oxidase, also found in most tissues. In this process, all of the physiological activity is lost and the end-product, 5-hydroxyindoleacetic acid (5-HIAA), is formed. In patients with malignant carcinoid marked elevation of this metabolite is found in the urine, and the determination of the 5-hydroxyindoleacetic acid level is now utilized as a diagnostic test.[18]

Function of Serotonin in Various Systems

As will be seen from the ensuing comments, much of the knowledge of any role which serotonin may or may not play in the various systems of the body is at a very tentative stage at the present writing. The consensus is that serotonin almost certainly has a role or roles, but the exact nature of its action in any organ system is still uncertain.

Cardiovascular Function.—The results of a great number of experiments conducted with the purpose of elucidating the action of serotonin on the cardiovascular system have produced such varied results that one writer[3] has utilized the term "amphibaric" to characterize its action. Present evidence does not permit any positive statement as to what role, if any, this substance plays under physiological conditions.

Experiments suggest that the most important factor determining the response of the cardiovascular system to serotonin is the degree of vasomotor tone. Measures which change the amount of neurogenic vasomotor tone change the response to serotonin. When vasoconstrictor neurogenic tone is high the response is hypotensive, and when low, hypertensive. This has lead to the interesting, albeit unproved, hypothesis that sero-

tonin provides the body with a sort of chemical buffering system for the control of neurogenic vasomotor tone.[3,19]

Renal Function.—Erspamer was the first to suggest that serotonin might be a renal hormone. There is still no definite answer to this postulate. The problem of whether serotonin normally exerts control on the caliber of the afferent arterioles has received the most attention. The latest studies seem to indicate that serotonin does reduce renal blood flow and glomerular filtration when given by infusion in normal persons. The method of this action is not known, and there is not yet sufficient evidence to state that serotonin functions as a physiological antidiuretic. For some reason, in humans the antidiuretic effect is most marked in those with diabetes insipidus.[3,20,21]

Function in the Brain.—Although most writers on the function of serotonin in the normal brain feel that it definitely plays some important role, the exact nature of this role remains obscure. The question of the physiological role of serotonin in mental processes is in an extremely confused state, and nothing of a definite nature can be stated with any certainty. The same may be said of its possible function or disturbance of function in mental disease.

The highest concentrations of this substance are found in those areas which contain central representation of autonomic activity, with the hypothalamus having the highest concentration of any area investigated. This, of course, would suggest that its actions lie primarily within that division of the nervous system, i. e., the autonomic.[22,23]

Recent work on the mechanism of action of the drug reserpine[24-26] lends strength to the supposition that serotonin is of importance in the nervous system. Reserpine has the property of inactivating the serotonin storage mechanism in body cells. It does this by converting serotonin from a bound to a free form, which is then rapidly destroyed by amine oxidase. It is still a moot question as to whether the pharmacological action of reserpine is to be attributed to the depletion of stored serotonin or to a continuous flow of active free serotonin, which acts on subcortical centers.

Function in Specific Disease Entities.—Much of the interest generated in serotonin during the past few years has come about directly or indirectly after the demonstration of elevated levels of serotonin in the blood and of 5-hydroxyindoleacetic acid in the urine of those patients with malignant carcinoid. Thus far this entity stands almost alone as the one pathological state in which a definite role can be attributed to serotonin without dispute.

So much has been written on the various manifestations of the functioning carcinoid[15,16,27,28] that a brief summary here of the changes in the skin should suffice. Kierland's[29] recent article describes them as follows:

> A transient cutaneous flushing which most frequently and severely affects the face. Cyanosis of varying degree may appear in spots in the regions of flushing. When the flush subsides, the central portions fade first. As the flushing becomes more chronic, telangiectasias become evident, and more persistent or permanent cyanosis and flush develop.

Less than half of patients with a malignant carcinoid demonstrate the symptoms known as the "carcinoid syndrome." Why some carcinoids are "functioning" and others remain asymptomatic has been the subject of much debate. Thorsen,[30] in a recent monograph on the subject, puts forth the following theory. It is felt that one of the chief sites of inactivation of serotonin within the body is the liver. Therefore, metastases which drain via the portal system would be less likely to produce symptoms than those which drain by way of the vena cava. Studies on a number of cases coming either to surgery or the autopsy table indicate that this may be the answer to this puzzling question.

Rotbart[31] tested two patients with elevated levels of 5-hydroxyindoleacetic acid in the urine by intradermal injection of serotonin. He found them hyper-reactive as compared with normal persons. The significance of this finding is obscure, but its possible use

as a skin test for carcinoid disease has been suggested.

A defect in the serotonin metabolic pathway has been demonstrated in another entity, phenylketonuria.[32,33] This rare disorder is characterized by a severe degree of mental deficiency, a defect of pigmentation, and the excretion of phenylpyruvic acid in the urine. Significantly lower values for serum serotonin and urine 5-hydroxyindoleacetic acid were found in patients with this disorder. This indicates a defect in tryptophan metabolism, which results in diminished serotonin production. While administration of serotonin to a few of these patients has not produced any dramatic change in their mental status thus far, it is felt that defective production of serotonin in phenylketonurics is an important factor in the pathological process.

Recently, Kowlessar and associates [34] have demonstrated increased excretion of 5-hydroxyindoleacetic acid in a series of patients with active nontropical sprue. Whether or not this increased excretion reflects a defect in the metabolism of tryptophan or is related to alterations in the mucosa of the small intestine is unknown. Previously, Anderson [35] reported on elevated levels of 5-hydroxyindoleacetic acid in the urine of those on a high-banana diet.

Although the possible role of serotonin in many other disorders (hypertension, anaphylaxis, renal disease, and mental illness, to mention only a few) has been widely discussed, the two entities mentioned (carcinoid disease and phenylketonuria) are the only ones at the present time in which definite abnormalities in serotonin metabolism have been conclusively demonstrated.

Function in the Skin.—No single agent has been found which accounts for the hyperemia and increased vascular permeability in the skin associated with many common reactions to injury. Therefore, much speculation has gone on concerning the possible role of serotonin in the inflammatory process.[36,37] The scattered and at times conflicting observations which have been made and the evident difference in various species make any summary and conclusions difficult at this time.

There is now little doubt that serotonin does play an important role in this respect in the skin of the rat.[12,25] Rowley and Benditt [4] have conducted experiments showing that agents which damage mast cells in the rat's skin release both serotonin and histamine and that the edema associated with mast-cell damage is mediated largely by serotonin. West and Parratt [8] have detected a substance in the edema fluid of rat's skin after injection of egg white, which has the properties of serotonin. Thus it is clear that serotonin may be responsible for vasodilation and increased permeability leading to edema.

Quantitative determination of serotonin in the skin of various animals has demonstrated that large quantities are found only in the skin of the rat.[8] As mentioned in the introduction, little or no serotonin is present either in the whole skin or in the separated parts in man. Human skin is deficient in serotonin even when abnormally large amounts of histamine are present or when the blood level of serotonin is excessive.

Inderbitzen [38] believes that he has demonstrated that intradermal injection of proteolytic ferments or proferments liberates histamine and probably also serotonin. The reaction was comparable with those seen in allergic reactions of the immediate type (Arthus).

Specimens of skin from human cases of urticaria pigmentosa [39] and from a mast-cell tumor failed to show elevated levels of serotonin. The serotonin level in the skin of a patient with carcinoid likewise was not elevated.[7] Examinations for bound serotonin were not done. Thus, the conclusion of most observers is that mast-cell proliferation in man is not accompanied by any appreciable increase in the skin content of free serotonin.

Although work so far has failed to ascribe an important role to serotonin in human skin physiology, it must be said, in all fair-

ness, that an extensive search for bound or masked serotonin has not yet been done.

Intradermal Injection of Serotonin in Human Skin

Review of Previous Reports.—Roddie [40] comments indirectly on the effects of serotonin on the cutaneous vessels when he describes the results of infusion of serotonin into the brachial artery of normal human subjects. This caused a decrease in forearm and hand blood flow, with marked reddening of the skin. He interpreted this result to mean that serotonin constricts vessels concerned with peripheral resistance but dilates the minute vessels of the skin.

In an article mainly concerned with the cardiovascular actions of serotonin, G. Reid [41] includes a good description of the effects of intradermal injection in normal subjects. The reaction consisted of erythema without itching or wheal formation. When the subcutaneous veins were visable and raised above the surrounding skin, a subcutaneous or intradermal injection caused them to disappear for distances up to several centimeters from the site of the injection. The constriction was so intense that massage of the veins with the finger could not force blood onwards past the constriction and raising the pressure in a sphygmomanometer cuff to 60 mm. did not cause distention of the constricted portions of the veins.

Rowley [42] tested human skin with serotonin on the dorsum of the fingers, the volar surface of the lower arm, and the lateral aspect of the upper arm. He found no difference in the reaction at any of these sites.

Lorincz and Pearson [43] are the most recent workers to comment on the intradermal action of serotonin. In a paper discussing their studies on axon reflex vasodilation and cholinergic urticaria, they describe the collapse of the surrounding large subcutaneous veins when serotonin was introduced by iontophoresis or intradermal injection. Previous injection of the areas with neostigmine (Prostigmin), hexylcaine (Cyclaine), atropine, 2-bromo-*d*-lysergic acid diethylamide (BOL-148), nicotine picrate, diphenhydromine (Benadryl), iproniazid (Marsilid), and saline produced no effect on the initially observed action. If a tourniquet was placed alongside the site of serotonin injection, the veins distal to the tourniquet failed to collapse.

Two facts suggest to them that serotonin is not the mediator of axon reflex and antidromic vasodilation. The first is that concentrations of serotonin required to produce visible erythema far exceed the reported maximum concentration of this substance in human skin. Second, when histamine flares are produced no vein collapse is noted, although concentrations far in excess of that required to give collapse would have to be present in order to produce the erythema.

Observations on Normal Persons (Tables 1, 2, and 3).—Thirty-four "normal" persons (no history of atopic dermatitis or allergy)

TABLE 1.—*Observations on Normal Persons*

Case No.	Erythema	Flare Diameter, Cm.	Duration of Reaction, Min.
1	++	3	100
2	++	3	90
3	++	4	105
4	+	2	75
5	++	3	95
6	+++	4	120
7	++	3	120
8	+++	3	110
9	+++	5	150
10	++	2	60
11	++	3	90
12	++	4	100
13	++	3	80
14	+++	3	100
15	+	1	30
16	++++	6	180
17	+++	5	120
18	++	3	100
19	++	4	90
20	++	4	110
21	+	2	70
22	++	3	95
23	+++	3	60
24	++++	5	100
25	++	3	50
26	+	2	30
27	+++	4	110
28	++	3	80
29	++	3	80
30	+	3	90
31	++	2	40
32	+++	4	160
33	++++	6	140
34	++	1	30

TABLE 2.—*Observations on Atopic Patients*

Case No.	Erythema	Flare Diameter, Cm.	Duration of Reaction, Min.
1	+++	5.0	10
2	++	2.0	10
3	++	3.0	30
4	+−	0.5	10
5	0	0.0	0
6	+	1.0	5
7	0	0	0
8	0	0	0
9	0	0	0
10	0	0	0
11	+−	1.0	8
12	0	0.0	0
13	++	3.0	20
14	0	0	0
15	+	1.0	10
16	+	0.5	15
17	0	0.0	0
18	+	0.5	15
19	++	2.0	30
20	0	0	0
21	+	0.5	10
22	0	0	0
23	0	0	0
24	+	0.5	15
25	+	0.5	10
26	++	1.0	20
27	++	1.0	20
28	0	0	0
29	0	0	0
30	0	0	0
31	+	1.0	10
32	0	0	0
33	+	1.0	20
34	+−	0.5	5
35	+	0.5	10
36	+++	2.0	30
37	+	0.5	10
38	+	0.5	5
39	0	0	0

were tested by intradermal injection of 0.1 cc. (10 μg. per cubic centimeter) of 5-hydroxytryptamine creatinine sulfate (serotonin) in the volar surface of the forearm (Table 1). The reactions were observed closely for the first 15 minutes and then at less frequent intervals until the reaction subsided. All persons tested gave essentially the same response qualitatively. Quantitatively there was fairly wide deviation as regards both intensity and duration of the reaction.

TABLE 3.—*Average of Totals*

	Normal (34)	Atopic (39)
Erythema, 1-4	2.3	0.8
Flare, cm.	3.3	0.7
Duration of reaction, min.	93.0	8.4

The reaction was as follows:

1. Erythema at the injection site.

2. An almost immediate flare about the injection site. This always appeared within 30 seconds of the time of injection. The size of this flare varied from 1 to 6 cm. in diameter. In most subjects tested, it was between 2 and 4 cm. in diameter. In every case the maximal extent of the flare was attained within five minutes of the injection time. The intensity of the flare was in direct relation to its size in each person tested. The duration of the flare varied from 30 to 180 minutes. This also seemed directly dependent upon the maximum diameter obtained and the intensity.

3. The wheal produced by the injection remained the same size or increased only slightly to the extent of 1-2 mm. over the initial size of 5-8 mm. No pseudopods were observed.

4. No subjective sensation was noted by any of the subjects tested.

5. In contrast to the findings of previous observers, no effect on the surrounding subcutaneous veins was noted.

6. Procaine injection locally inhibited the flare response where the procaine was injected. This is similar to the inhibition of the histamine flare with procaine and probably represents interference with an axon reflex type of flare response.

Observations on Patients with Atopic Dermatitis. — Thirty-nine patients with atopic dermatitis were tested by intradermal injection of 0.1 cc. (10 μg. per cubic centimeter) of 5-hydroxytryptamine creatinine sulfate in the volar surface of the forearm (Table 2). In most cases the injections were made in areas uninvolved by the disease process. The reactions were observed until they had subsided.

In 17 of these patients there was no visible reaction when serotonin was injected into the skin. The remainder of the patients showed a sharply diminished response to serotonin. Rarely was the erythema greater than + (grading from + to 4+), and the minimal erythema that developed was extremely evanescent in nature. There was no correlation between the intensity of the reaction and the severity of the dermatitis.

Comment

Rothmann and Bloom [44] have recently reviewed the subject of increased vasoconstric-

tion in the atopic person and conclude that this tendency is not due to increased excitability of vasoconstrictor nerve fibers but to an increased responsiveness of the contractile elements of the blood vessel walls. They would like to assume that increased vasoconstriction is one of the stigmata of the atopic diathesis.

This tendency has been noted in the response of the atopic to stroking, heat, cold, histamine, nicotinic acid esters, and acetylcholine.[45-49] Presumably our observations are a further demonstration of this facet of the atopic diathesis.

This demonstration of minimal or absent vasodilation with serotonin emphasizes the basic physiologic difference between vascular responses in normal persons and in atopic patients. This is most probably an inherited abnormality, and one wonders of course what these fundamental physiologic abnormalities have to do with development of atopic skin disease. Previous emphasis on psychogenic and allergic factors in this disease have been of very limited help in understanding the basic mechanisms of atopic dermatitis.[50-51] Perhaps the painful process of unfolding abnormal fundamental physiologic responses in this group will lead us some day to the etiology.

Summary

The physiologically active agent serotonin (5-hydroxytryptamine) has received tremendous interest since its isolation just 10 years ago. Its metabolism in man from the major precursor, tryptophan, to the final excretion product, 5-hydroxyindoleacetic acid, is now well established.

Much work on its possible role or function in the various systems of the body (cardiovascular, renal, nervous) has yielded few definite data at this writing. However, few workers in the field doubt that a role or roles exist.

In two disease entities definite abnormalities in serotonin metabolism have been conclusively demonstrated. Thus one finds an overproduction of this metabolite in patients with the carcinoid syndrome and an underproduction in phenylketonurics.

Its function or lack of function in the skin of man is uncertain. There is little doubt of its importance in the skin of the rat. Perhaps when methods of measuring bound serotonin are evolved its role in human skin physiology can be more accurately determined.

In our experiments serotonin was injected intradermally in 34 normal subjects and in 39 patients with atopic dermatitis. The reaction of the skin of the normal person consisted of local erythema and a flare, without wheal formation or subjective sensation. By contrast, in the skin of the atopic, there was, in many cases, no visible reaction. When a reaction did occur it was similar in nature to the normal response but greatly diminished in intensity and evanescent. This is considered by us to be a further demonstration of the increased tendency to vasoconstriction manifested by those with the atopic diathesis.

Dr. John Haserick and his staff at the Cleveland Clinic supplied some of the patients for this study.

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Treatment of Acute Parapsoriasis with Corticotropin (ACTH)

Report of a Case

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Acute guttate parapsoriasis, or pityriasis lichenoides et varioliformis acuta of Mucha-Habermann, is an entity better known for the length of its name than for the importance of any clinical information concerning it. Our studies in the past several years, and recently those of Piérard and Van Steenbergen,[1] have led us to the conclusion that microscopic hemorrhage is the typical histologic finding in this entity and that the hemorrhage occurs on the basis of intense inflammation of capillaries. Szymanski[2] recently discussed a large series of these cases on the basis of allergic angiitis as the etiologic factor. The variable clinical lesions could be explained on such a basis.

While this progress in the basic understanding of some of the clinical and histopathologic features of the disease was being made, no progress in treatment has been recorded for many years. Canizares[3] reported success with use of calciferol (vitamin D_2), and many combinations of vitamin D and antibiotics have been used by other authors.[4] Degos and associates[5] reported a case of chronic parapsoriasis in which the condition converted to an acute form; intensive treatment with antibiotics and steroids resulted in recovery in the sense that the eruption once again reverted to the typical lesions of chronic parapsoriasis. While other authors have noted this conversion of chronic to acute parapsoriasis, Ingram[6] did not mention such a change in his study, in which he separated the acute and chronic forms of pityriasis lichenoides from the major group of parapsoriasis.

The following case is reported as representing the first instance of successful treatment of acute parapsoriasis based on the concept of the disease as an anaphylactoid purpura (allergic angiitis).

Report of Case

A 31-year-old man was seen at the Mayo Clinic in May, 1958. He had noted a papulovesicular plaque on the right lower abdominal wall 18 days before admission. Four days later, this had begun to spread over the trunk and to the extremities. Two days before admission, the palms, soles, and face had become involved. The patient had continued to work, and his sleep had not been interrupted. He felt well and had not noted any fever. A history of exposure to drugs, chemicals, or insects could not be obtained; he had not experienced any allergic reactions in the past.

Examination disclosed a universal, maculopapular, vesicular, and hemorrhagic eruption in all stages of development. Some of the papules had progressed to superficial hemorrhagic necrosis. Lesions were present on the hard palate and on the palms and soles. His temperature was 98.8 F. Lymphadenopathy or palpable enlargement of organs was absent.

The erythrocytic sedimentation rate was 23 mm. during the first hour (Westergren method). Grade 1 erythrocyturia was present. Hematologic studies, including hemoglobin, blood cell counts, a differential count, and a platelet count, showed normal results. The prothrombin, bleeding, and clot-retraction times were normal. A serologic test for syphilis (VDRL) was nonreactive. A thoracic roentgenogram was normal. Tissue obtained at punch biopsy was cultured, revealing Staphylococcus pyogenes var. aureus in large numbers. The staphylococci were sensitive to penicillin (1 unit

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Mayo Clinic and Mayo Foundation. Section of Dermatology (Dr. Winkelmann) and Fellow in Dermatology, Mayo Foundation (Dr. Lorenc). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

per milliliter), tetracycline (3μg. per milliliter) and erythromycin (1μg. per milliliter). Two blood cultures gave no growth of organisms. It was considered that the staphylococci were contaminants because of their pronounced sensitivity to antibiotics and the absence of bacteremia. The clinical impression was acute parapsoriasis. Biopsy confirmed this.

The patient was hospitalized. His temperature during the first 24 hours varied between 99 and 100.8 F. He complained of mild malaise on the first day. He was given 10 units of corticotropin (ACTH) intravenously and diphenhydramine (Benadryl) hydrochloride by mouth. The following day he had a few more purpuric spots on the legs and feet; he received 40 units of corticotropin intravenously. The following day he had improved; he again was given 40 units of corticotropin intravenously. Each of the subsequent four days he was given 20 units of corticotropin intravenously. He was dismissed on the eighth day of hospitalization, at which time his condition was greatly improved (Figs. 1 and 2).

Nine months later, the patient did not have any lesions and was healthy in all respects.

Comment

The patient's lesions resolved almost without residua except for a faint hemosiderin macule. Because he has not had any relapse and his health has been maintained in such an excellent state, it is presumed that this entity represented some form of toxic vascular episode that can be safely and readily treated by means of steroids. We have seen other patients with Mucha-Habermann disease who have been given steroid therapy without benefit. In general, however, the material given represented a

Fig. 1.—The generalized distribution of the lesions. (*a*) Appearance on admission. Note involvement of palms. (*b*) Appearance after one week of treatment with corticotropin. The lesions have undergone involution.

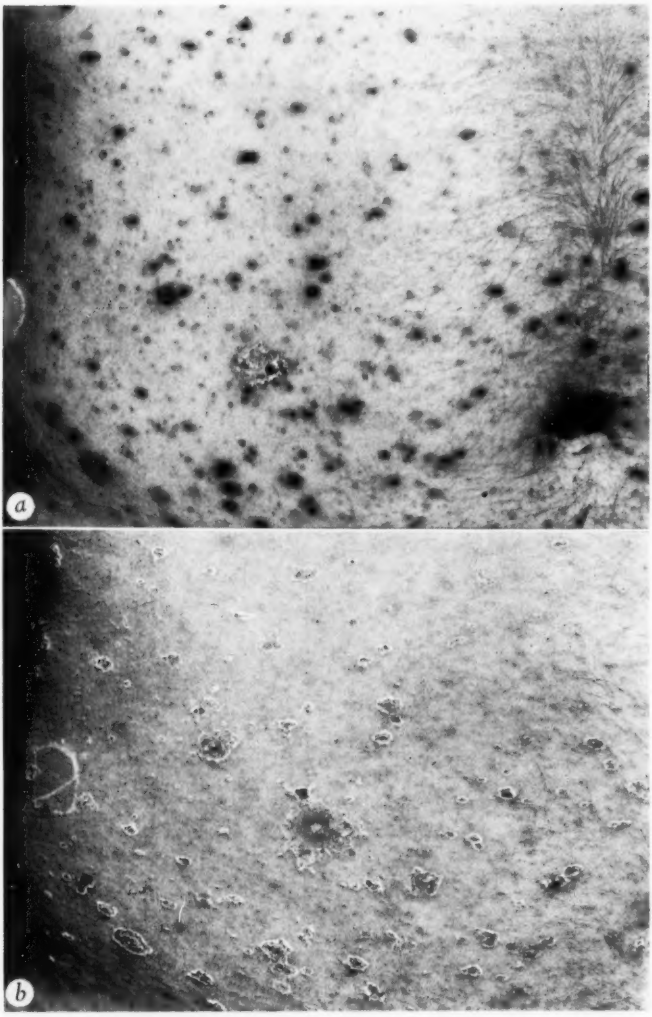

Fig. 2.—(*a*) The polymorphous nature of the eruption on admission, ranging from papulovesicles to hemorrhagic necrosis. (*b*) Appearance one week later, showing pronounced degree of involution after use of corticotropin.

cortisone equivalent that seldom was more than 100 mg. per day. This amount apparently is not enough to cause the eruption to undergo satisfactory involution. If steroids are to be used, they should be used vigorously in large doses; their administration should be tapered off quickly after the first two weeks.

This patient's dramatic response underlines the importance of early and vigorous treatment if the eruption is to be healed quickly and easily. If this disease represents a form of allergic angiitis, the response of this patient was a foregone conclusion in terms of prior experience with such an entity.[7] This therapeutic response to steroids further confirms the clinical and histologic observations that point to intense vasculitis as the basis for the polymorphous cutaneous reactions.

The histologic appearance of the lesions in this case parallels perfectly the illustrations of Piérard and Van Steenbergen and is consistent with our own experience in acute parapsoriasis. Figure 3*a* illustrates the necrosis and vasculitis, with formation of a

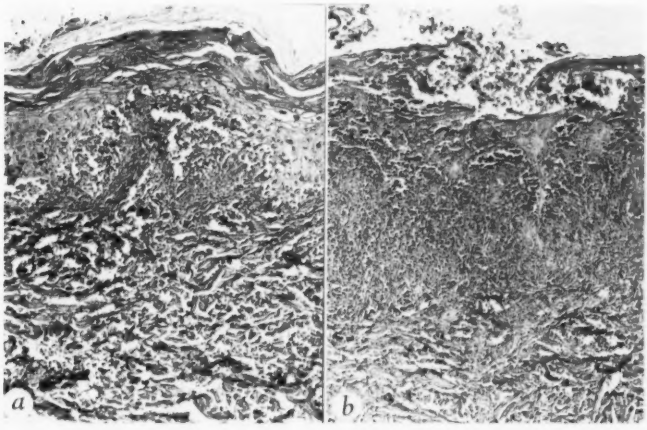

Fig. 3.—(*a*) Section of papulovesicle, demonstrating the underlying vasculitis and a subepidermal bulla secondary to papillary necrosis. (*b*) Section of an infarcted zone, showing the superficial hemorrhagic crust and necrosis of both papillary dermis and the epidermis (both, hematoxylin and eosin; reduced from ×100).

subepidermal vesicle. The superficial necrosis and edema become so intense that the papillary dermis is involved also (Fig. 3*b*). The angiitis is not distinguished so readily in this condition as it is in some forms of angiitis of the skin in which the necrosis is of slower generation, as in the nodular allergy of Gougerot or in erythema elevatum diutinum.

One must be entirely sure of the diagnosis before treatment is begun. Clinical findings are usually diagnostic, and biopsy of the skin is helpful. It is extremely important not to mistake this entity for some infectious process. The presence of vesicles occasionally might cause some confusion with simple diseases such as varicella. Under these circumstances, of course, steroid therapy would be contraindicated. Therefore, appropriate cytologic, histologic, and bacteriologic investigations for the causative organisms should be undertaken and pursued diligently so as to confirm the diagnosis as quickly as possible.

Summary

A patient who had lesions that fulfilled the clinical and histologic criteria of acute parapsoriasis was treated with corticotropin (ACTH) on the basis that this disease represents an acute episode of allergic angiitis. The treatment was followed by complete resolution of the lesions in one week and lack of recurrence during a subsequent follow-up period of nine months.

Mayo Clinic.

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Macular Atrophy Following Infection

Report of a Case

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In 1891, Schweninger and Buzzi [1] originally described macular atrophy under the title, *Multiple Benign Tumor-like New Growths of the Skin.* Since then, the few and isolated case reports of the condition have failed to bring forth any substantial evidence of etiologic relationship. The clinical features of the various reported cases of macular atrophy are strikingly similar to the classic description of Schweninger and Buzzi.[1] Combes [2] and later Chargin and Silver [3] showed that both primary and secondary macular atrophy have a similar histologic picture and suggested that toxic substances, whatever their nature, may be assumed to play a role in the production of the degenerative process. Scull and Nomland [4] believed that secondary macular atrophy, irrespective of the causative disease, occurs subsequent to a subclinical destruction of the elastic tissue in the upper dermis by an inflammatory infiltrate. Butterworth [5] reported a case of primary macular atrophy in which he suggested the possibility that a low-grade infection may be related in some way to the macular atrophy.

The following case may show a possible etiologic relationship in primary macular atrophy, and it appears to be solely a cutaneous involvement.

Report of Case

History.—A white youth, aged 18 years, first noticed the development of papules and tumor-like lesions over the trunk, shoulders, arms, neck, and lower face in January, 1956. The onset was rather sudden, and subsequently new lesions gradually developed. The older lesions became flattened after several weeks, and some eventually became depressed, scar-like areas. The condition was asymptomatic.

Immediately before the onset of this condition the patient had an acute tonsillitis for which he was hospitalized. He had also had chronic, recurrent abscesses of the teeth and gums since October, 1955.

He had always been in good general health, and there was no history of any antecedent skin eruption. As a child he had measles, chickenpox, and scarlet fever. Family history was noncontributory and his parents were living and well.

Physical Examination.—The patient was first examined in March, 1956. He was a well-developed, muscular, white youth, appearing mentally alert and in good health. The height was 69 in., and the weight, 180 lb. The temperature ranged from 98.2 F to 99.0 F. The pulse varied between 70 and 80 per minute, and respirations were 14 per minute. The blood pressure was 110 systolic and 78 diastolic. A complete physical examination revealed normal findings except for the skin findings and oral pathology. Ophthalmologic consultations reported normal vision and no evidence of disturbance of the elastic tissue in the choroids of the eyes.

Oral Examination and Dental Consultation: Chronic hypertrophic gingivitis and multiple gingival abscesses were present on the left lower jaw. Dental x-ray films showed two apical abscesses involving both left lower molar teeth.

Examination of the Skin: There were multiple bean-to-coin-sized lesions distributed in the skin lines of cleavage over the trunk, shoulders, arms, neck, and lower face. The more recent lesions were bluish white papules and nodules, rubbery in consistency, and elevated above the skin surface, and a faint erythema with fine telangiectasia could be detected in some of them. There was no apparent change in the overlying epidermis. The older lesions were more flaccid, bladder-like protrusions, and the overlying epidermis appeared atrophic, white, and wrinkled. With the tip of the finger, many of the older lesions could be inverted below the surface of the skin. The protrusion reappeared like a ventral hernia when the finger was released. A few of the old lesions had involuted, leaving

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flaccid, depressed scars (macular atrophy). These were pronounced over the neck and trunk.

Laboratory Studies.—Laboratory tests findings were all within normal limits. Urinalysis was normal in gross, microscopic, and chemical studies. The blood count revealed 4,500,000 red cells per cubic millimeter, with 14.8 gm. of hemoglobin per 100 cc. The hematocrit was 46%. There were 8,100 white cells, of which 66% were polymorphonuclears, 32% lymphocytes, and 2% eosinophils. The sedimentation rate was 18 mm. per hour. Repeated blood Wassermann and Kahn tests were negative. Liver-function tests revealed normal results and included the cephalin flocculation, sulfobromophthalein excretion, and thymol turbidity tests. The alkaline phosphotase was 3.18 U. (Bodansky), and the total serum proteins were 8.05 gm., with 4.25 gm. of albumin and 3.81 gm. of globulin per 100 cc. Blood urea nitrogen was 19.5 mg. per 100 cc., and the fasting blood glucose was 106 mg. per 100 cc. (Folin-Wu). Serum calcium was 5.3 mEq., and serum phosphorus was 2.0 mEq. per liter. The roentgen examination of the chest gave no evidence of tuberculosis or other pathologic condition. Mantoux tests, performed with dosages of 0.01 and 0.1 of old tuberculin, gave no reaction. Electrocardiogram readings were normal. Bacteriologic and culture studies of the gingival abscesses and apical abscesses revealed Streptococcus viridans not sensitive to penicillin and sensitive to oxytetracycline, chloramphenicol, erythromycin, and bacitracin.

Histologic Examinations.—A muscle biopsy was performed on the left gastrocnemius muscle. Histologic examination revealed normal muscle and blood vessels, with no evidence of elastic tissue alteration. The skin biopsy was a complete excision of an early lesion on the abdomen. The tissue was stained with Weigert's stain. The epidermis was slightly thinner over the lesion, and there was some flattening of the rete pegs. Fragmentation and disappearance of elastic tissue were noted throughout the dermis of the lesion. Collagen tissue appeared more delicate but was otherwise unaffected. There was no evidence of edema, and there was only slight evidence of round-cell infiltration about blood vessels and glands of the skin.

Clinical Course.—The patient was followed for two years and was examined monthly. The infected teeth were extracted and the gingival abscesses were incised and drained in May, 1956. Oxytetracycline was administered in the dosage of 250 mg. q. i. d. for 10 days prior to dental surgery and for 10 days afterward. All of the oral infection was eradicated, and the patient had no evidence of oral infection thereafter. New lesions continued to appear until July, 1956. Thereafter, there was no evidence of the development of the characteristic early lesions, but the preexisting lesions continued to involute and become more pronounced as the macular atrophy progressed. The characteristic phenomena of herniation developed in most of the preexisting lesions. Older lesions gradually became depressed below the surface of the skin. The patient thought he was developing more lesions because the preexisting early lesions, which at first were unnoticeable, became more prominent. The total number of lesions, over 200, had not increased in number after July, 1956.

Comment

This case is presented primarily because of its rarity and the paucity of reports in

Fig. 1.—Typical distribution of lesion along skin lines of cleavage.

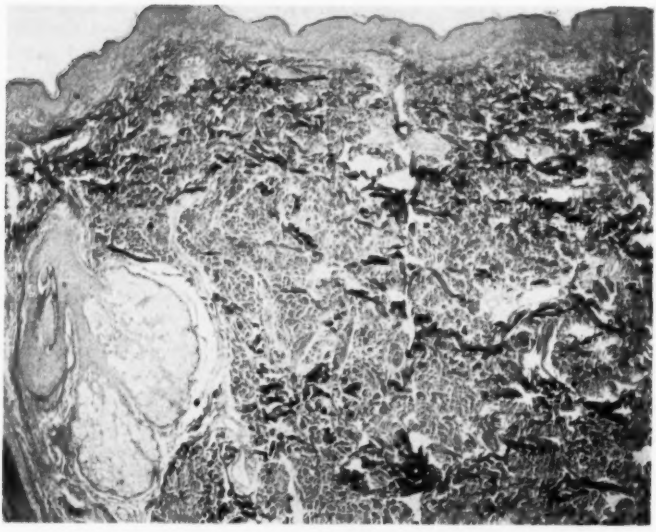

Fig. 2.—Weigert preparation illustrating fragmentation and scarcity of elastic tissue in the dermis of the lesion.

the literature. The possibility of bacterial foci of infection being the etiology in primary macular atrophy has not been given more than speculation. The development of this condition during the course of an active, chronic S. viridans infection of the teeth and gums and also after an episode of acute tonsillitis might possibly implicate a bacterial etiology. The fact that new lesions failed to develop after the oral focus of infection was completely eradicated would also favor this as the etiologic agent.

It is known that many infections may have a damaging influence on the cutaneous elastic tissue, and this may be manifested in the development of striae during the course of the illness. These infections include diseases such as typhoid fever, dysentery, paratyphoid, typhus, rheumatic fever, leprosy, syphilis, and other infections. It is conceivable that bacteria or their products could produce focal degeneration of the elastic tissue in the skin, thus producing the lesions of multiple benign tumor-like new growths of the skin. There is doubt whether there are any clinical differences between primary and secondary macular atrophy. The histologic pictures, in either condition, are similar. For these reasons it is probable that macular atrophy is always secondary to some underlying disease, which liberates a toxin capable of producing focal cutaneous elastic tissue degeneration.

Previous reports have made no mention of normal findings in the elastic tissue of the choroids and arteries in muscle. It appears that this condition is purely a cutaneous alteration in the elastic tissue, with no evidence that the elastic tissue in other organs is involved.

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Lichen Myxedematosus (Papular Mucinosis Dalton and Sidell)

Report of an Additional Case

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Lichen myxedematosus (papular mucinosus) is a relatively uncommon disease. Since Dalton presented the first American case of lichen myxedematosus at the Dermatological Conference of the Mississippi Valley and Central States Dermatological Association on Feb. 9, 1941,[1] a few additional cases were reported in the American literature.[2,3] In the European literature one encounters but rarely studies on lichen myxedematosus.[4-7] Hence, the report of an additional case of lichen myxedematosus observed by us in the summer of 1957 is deemed worthy of publication.

Report of Case

A 55-year-old white widow whose occupation was that of office cleaning developed a skin eruption on the dorsa of the hands and wrists in the fall of 1956. The eruption then spread to involve the skin of the forearms, arms, thighs, knees, and sternum. The affected regions then became coarse, rough, thickened, and red. She complained of persistent burning and itching. During the ensuing winter, she noticed that her fingers would turn blue and feel numb when exposed to cold. This was localized to the distal two phalanges of the fingers of both hands. On warming, the color and sensation returned to normal. After the onset of her skin eruption she became somewhat nervous and worried, slept and ate poorly, and lost about 20 lb. in weight. She had received occasional therapy for hypertension over the previous 12 years. Obesity had been present for over 25 years, and her eyes had been prominent since early childhood. She denied any other serious illness.

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From the Department of Dermatology (Service of Dr. Zakon), and the Department of Pathology (Israel Davidsohn, Director) Mount Sinai Hospital. Dr. Henry Grinvalsky is now pathologist at Saint Michaels' Hospital, Stevens Point, Wis.

General physical examination revealed an obese white woman, weight 186 lb., pulse 80, and blood pressure 164/98. The eyes were prominent, but there was no perceptible widening of the palpebral fissure and no lid lag. The mucous membranes of the mouth had a pebbly appearance. A left inguinal hernia of many years' duration was present. The reflexes were physiological, and there was no tremor of either hands or tongue. The remainder of the general examination was negative. Examination of the skin revealed the primary lesion to be an irregular flat papule 3 to 6 mm. in diameter. Coalescence had produced an extensive lichenoid eruption involving the hands, wrists, forearms, arms, thighs, knees, and sternal region. A definite linear distribution of the papules was present. Color in the affected areas varied from red to yellow, and on diascopy the papules were yellow-white. The involved areas presented the sensation of thickening of the epidermis, but there was no resistance or hidebound feeling on palpation. Despite the redness, there was no sensation of increased heat, and there was no pitting.

Laboratory Studies.—The results of routine urinalysis, blood cell count, serologic test for syphilis, and chest x-ray were all normal or negative. A basal metabolism test showed a +30 and +27 reading.

Biopsy specimens of skin removed from the region of the left thigh were studied by one of us (H. G.).

Histopathologic and Histochemical Studies.—Sections of the skin from the thigh revealed mild hyperkeratosis and mild to moderate acanthosis. The epidermis was irregularly elevated by edema and focal proliferations of fibroblasts concentrated principally about superficial ectatic capillaries. These focal aggregates effaced rete pegs.

Elsewhere in the superficial corium ectatic capillaries were associated with a mild perivascular inflammatory reaction, consisting principally of lymphocytes and monocytes. The basal layer of the epidermis was focally hyperpigmented, and an occasional melanophore was present in the subjacent corium. The collageneous fibers of the mid and deep corium were separated by edema spaces which contained a faintly basophilic, granular coagulum.

In mucicarmine preparations the granular coagulum stained with a pale rose tint. When acid mucopolysaccharide technique of Rinehart and Abul-Haj [11] was applied to preparations, the granular coagulum gave a strong and sharply contrasting positive reaction which disappeared in sections subjected to hyaluronidase digestion prior to staining. An equivocal mucicarminophilia was present in the edematous, fibroblastic foci in the superficial corium, and there was no positive response to the acid mucopolysaccharide stain. Giemsa preparations revealed no notable increase of mast cells.

Discussion of Histopathologic Features.—The histopathologic features of the case herein reported appear similar to those described in Case 3 reported by Montgomery and Underwood.[3] In their case the superficial edematous papules failed to reveal the presence of mucicarminophilia, while mucin appeared to be distributed diffusedly throughout most of the cutis. The results of the Hotchkiss and McManus stains were indeterminate. In other reported cases of lichen myxedematosus, the demonstration of mucicarminophilic material has been difficult or equivocal, and the use of a strong solution of mucicarmine, preferably without counterstain, has been advocated by Montgomery. The crisp and unequivocal reaction obtained by the use of the Rinehart and Abul-Haj acid mucopolysaccharide stain may prove useful in evaluating other cases of the myxedematous (mucoid) states. The disappearance of the positive reaction after hyaluronidase digestion in our case lends some support to the proposal that the edema in lichen myxedematosus is related to an increase in hyaluronic acid.

Comment

Since the comprehensive reviews in 1953 by Dalton and Seidell,[1,2] and by Montgomery and Underwood,[3] little has been added to our present knowledge. The latter authors reported three cases in detail and presented brief reports of several other cases. Clinically, lichen myxedematosus must be distinguished from scleroderma, neurodermatitis, lichen ruber moniliformis, myxedema, amyloidosis, lichenoid tuberculids, and other lichenoid eruptions.

There were several clinical points of similarity between our case and previously reported cases in that the initial lesions appeared on the dorsa of the hands and wrists; there was laboratory evidence of elevated basal metabolic rate without clinical evidence of hyperthyroidism, and there was a history of Raynaud's phenomenon.

Despite the fact that there has been considerable research on the metabolism of mucopolysaccharides, until now there have been no definite conclusions as to the etiology and pathogenesis of lichen myxedematosus. The most generally accepted theoretical explanation is that the mucinous edema is due to the edema-producing action of the thyroid-stimulating hormone secreted by the anterior pituitary gland. Tappeiner [8] found abnormal serum-globulin values in a case of lichen myxedematosus in which the liver was enlarged, and studies indicated disturbed liver function. In his case, also, the B. M. R. was elevated, but clinical findings did not substantiate the diagnosis of hyperthyroidism. Tappeiner [8] postulated that new protein-like mucoid substances were formed and deposited in the walls of smaller vessels, thus causing slowing of circulation, with extravasation into the tissues resulting in the precipitation of mucoid substances. The most extensively studied case of lichen myxedematosus in the literature is one of those reported by Dalton and Seidell.[2] Electrophoretic studies of serum proteins in this case revealed decreased albumin and increased globulin values. However, a complete liver profile failed to explain these abnormalities. Tappeiner's [8] case showed similar electrophoretic studies. Tappeiner's [8] hypothesis of the pathogenesis has some credence in view of the autopsy findings in a case of lichen myxedematosus reported by McCuistion and Schoch.[13] In this report, the tissues studied were from a case diagnosed as lichen myxedematosus by Montgomery and Underwood in 1950. The most significant findings were those of deposition of mucin, mainly in the skin, but also in the various layers of the blood vessels and in the perivascular connective tissue of the heart, kidney, pancreas, and adrenal gland. Deposits of mucin were not found in the brain, thyroid, lymph nodes, lungs, liver, or gallbladder. Montgomery had previously reported that postmortem examination in one of his cases failed to reveal any evidence of myxedematous change in any of the internal organs.

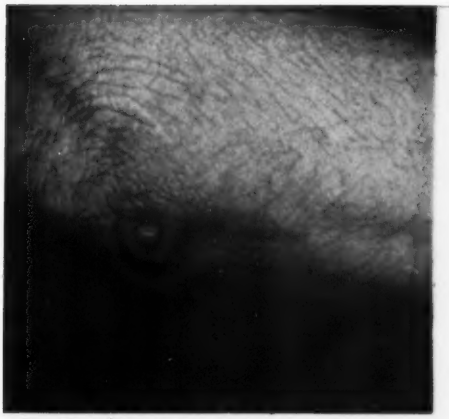

Fig. 1.—Clinical photo demonstrating numerous discrete or coalescing flat papules on the knee and leg.

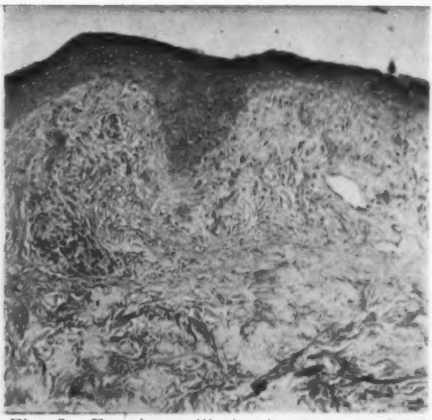

Fig. 2.—Ectatic capillaries in the superficial corium are surrounded by edema separating proliferating fibroblasts. Mayer mucicarmine stain; reduced ⅛ from mag. × 96.

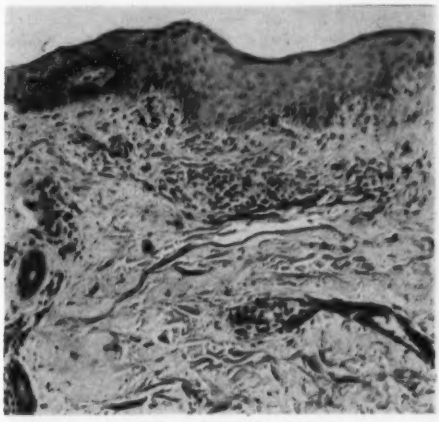

Fig. 3.—A mild perivascular inflammatory reaction consists of lymphocytes and monocytes in the upper corium. Giemsa stain; reduced ⅛ from mag. × 96.

Fig. 4.—Collagenous fibers separated by edema and the spaces contain a mucicarminophilic granular coagulum. Mucicarmine stain; reduced ⅛ from mag. × 120.

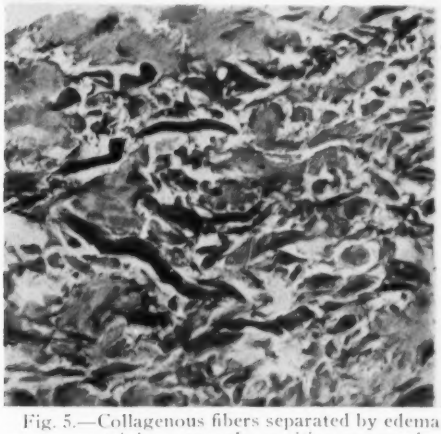

Fig. 5.—Collagenous fibers separated by edema spaces containing strongly positive mucopolysaccharide. Rinehart-Abul Haj acid mucopolysaccharide stain; reduced ⅛ from mag. × 120.

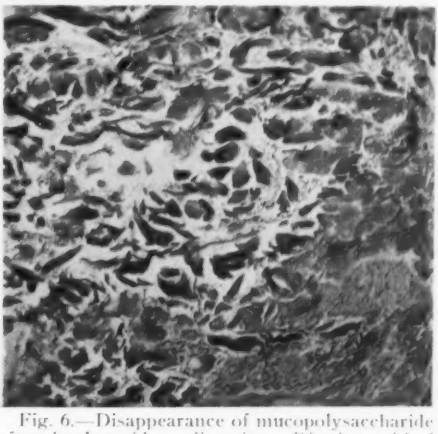

Fig. 6.—Disappearance of mucopolysaccharide after hyaluronidase digestion. Rinehart-Abul Haj acid mucopolysaccharide stain; reduced ⅛ from mag. × 120.

Concerning the theoretical explanation that lichen myxedematosus either is due to an imbalance of hyaluronidase and hyaluronic acid or that a blocking agent to hyaluronidase exists, it may be stated that hyaluronidase has not been conclusively demonstrated to occur in the mammal in locations other than in the testicular tissues. It is presumed that other enzyme systems are concerned with the synthesis and breakdown of mucopolysaccharides, but their exact nature is as yet unknown.[11]

Conclusions and Summary

Lichen myxedematosus is an uncommon disease. While the histopathology in all of the mucoid diseases is characterized by excess accumulation of mucin, the differentiation from myxedema and from pretibial myxedema is made on the basis of absence of thyroid and other endocrine disease. Clinical diagnosis without histopathologic studies is practically impossible. The use of the AMP stain as described not only is effective but allows unmistakable interpretation.

A case of lichen myxedematosus is recorded with a brief discussion of current literature.

1 N. Pulaski Road (24)

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The Pathogenesis of Superficial Fungous Infections in Cultured Human Skin

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In a living host the selectivity of dermatophytes for the keratin-containing dead outer structures of the skin is so extreme as to engender the terms keratinophilic and necrophilic for these organisms. The present study provides data to suggest that there are humoral factors which ordinarily bar invasion by dermatophytes but that under appropriate circumstances the organisms will readily invade living nonkeratinous skin.

The superficial habitat of the ringworm fungi is not a result of favorable nutritional factors in the keratinous layers. In the test tube, dermatophytes grow as vigorously in other media as they do in one containing only keratinous materials, such as powdered callus, or hair or nail clippings. Jacobs and Lorincz found little difference between growth of dermatophytes on the corium side or the cornified side of buttons of excised and killed human skin.[12] Nonetheless, even when the organisms gain entrance through a follicle into the deeper tissues, as in the nodular granulomatous perifolliculitis recently elucidated by Wilson et al.,[30] the dermatophytes fail to become truly invasive. Newcomer et al.[20] showed that they would grow deep inside the body within a "granuloma pouch," but even here penetration and spread to other viable tissues did not occur. Thirty years ago, Jadassohn and Sulzberger [13] found that although the dermatophytes remained viable and pathogenic for long periods in organs and body fluids of living animals, they would multiply and propagate only in dead tissue, namely, the stratum corneum, hairs, and nails.

It would seem that some host factor confines the dermatophytes to their superficial position. From observing the sharp limit of penetration of hyphae into growing hair, Kligman [15] postulated the presence of a determinant biochemical substance acting as an inhibitor. Just a year ago, Lorincz et al.[19] reported that fresh human serum contained a factor which would prevent the growth of dermatophytes within a dialysis membrane suspended in the serum. They postulated that such a factor could prevent invasion of the fungi below the epithelial "barrier" of the skin. That human serum had a fungistatic effect was suggested in a number of earlier studies: Jessner and Hoffmann,[14] in 1924; Ayres and Anderson,[3] in 1934, and Peck, Rosenfeld, and Glick,[21] in 1940. This earlier work was unknown to us at the time our own interest in the problem was excited by finding that dermatophytes did not thrive on a tissue-culture medium (Fig. 1). The agar medium we were using contained all nutrients necessary for the growth of the most fastidious microorganisms or animal cells, and it seemed paradoxical that the omnivorous fungi would not grow well. Further studies soon demonstrated that the human serum component was responsible for the inhibition. In another report details of the serologic studies of the direct effect of serum against dermatophytes and in vitro are presented

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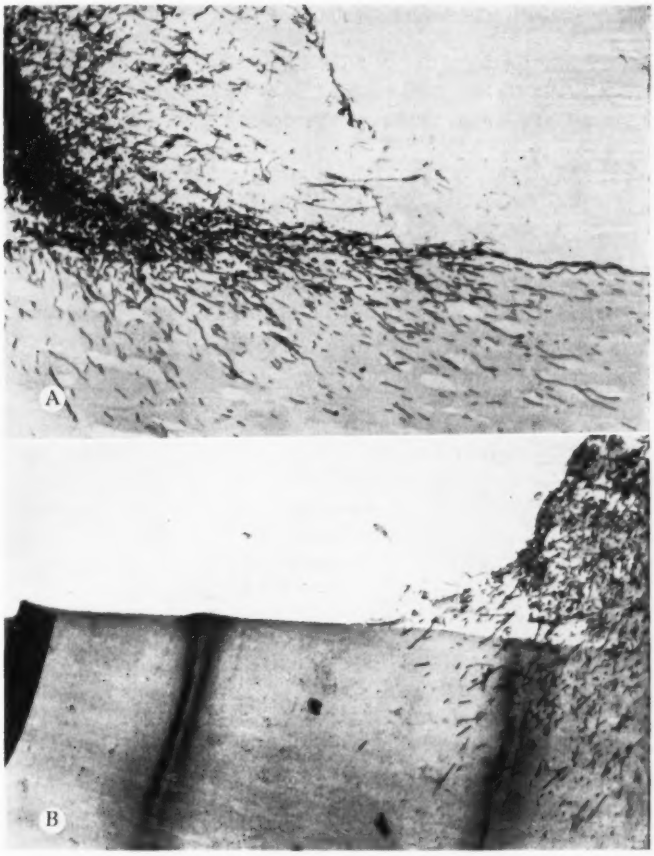

Fig. 1.—*A*, histologic section of mycelial pellet of T. rubrum on Sabouraud's agar at 35 C for 40 hours. *B*, same as *A* but 80% normal human serum agar. Both surface spread and mycelial invasion are reduced.

(Roth et al.[23]). In the present paper we are reporting observations on the way serum antifungal activity manifests itself against dermatophyte infections in organ cultures of full-thickness human skin.

There have been attempts to study fungi in ordinary single-layered cell cultures of human skin (Hu et al.[11]), but the results do not simulate human infection. It was felt that if thin but full-thickness sheets of skin could be grown in the laboratory on the surface of nutrient media with their outer epidermal surface exposed to the air, infection might mimic that in the living host. The embryologists have been using such techniques with fetal tissues for many years. Fell and Robison[8] used the surface of naturally clotted media in concave watch glasses; Spratt[26] used agar media, and recently Chen[5] further simplified the technique of surface culture of fetal organs by growing them on the surface of lens paper floating on a nutrient medium. We performed a number of experiments with these methods (Fig. 2) as well as with various fabrics[24] or a Milipore membrane[1] floating on media and with skin on the surface of a small piece of sponge partly submerged in the medium.[17] Although all methods were used with considerable success, the most convenient and regularly reliable were the lens-paper or the agar methods, which are described as modified in our laboratory.

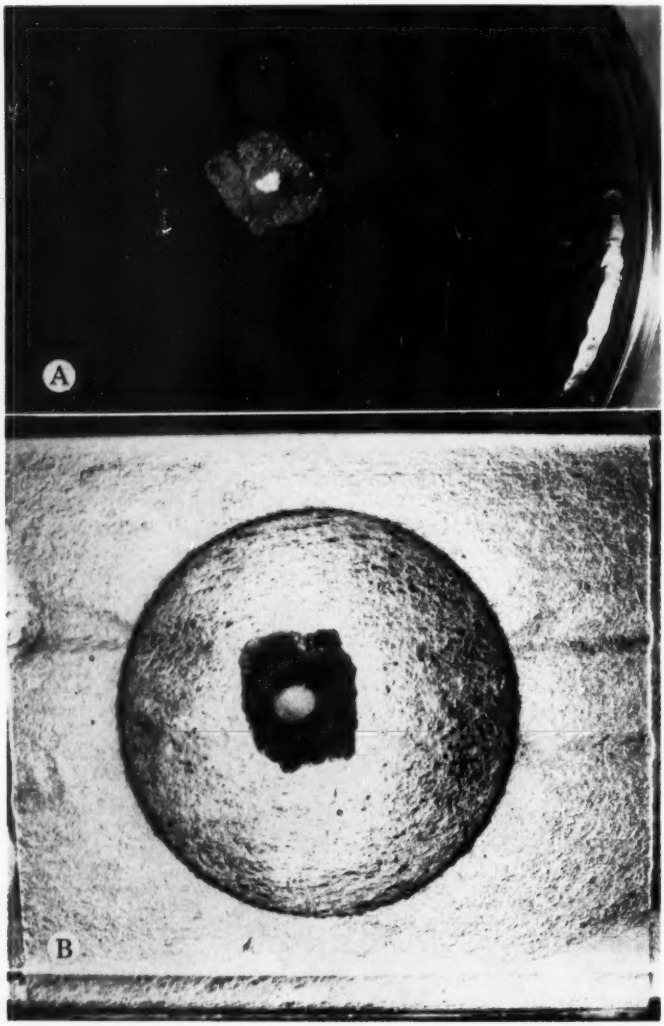

Fig. 2.—*A*, a pellet inoculum of fungus on a thin sheet of skin on an agar medium. *B*, a pellet inoculum of fungus on a thin sheet of skin on lens paper covering the well of liquid medium.

Materials and Methods

The normal human skin that was used for most experiments was the prepuce obtained at circumcision of newborn infants. Naturally infected skin was obtained from adults by surgical excision of a clinically typical lesion. Prior to use, the specimens were stored at 4C, thoroughly wetted but not floating in Hank's solution containing 1.0% glucose and 500μg. neomycin and 500 units of bacitracin per milliliter. These antibiotics were used because staphylococcal contamination with organisms resistant to penicillin and streptomycin were frequently encountered early in the work. Studies by Cruickshank and Lowbury[6] and by Hu et al.[10] have shown neomycin and bacitracin to be nontoxic at the concentrations chosen. Whenever possible the skin was used within 24 hours or less of its removal. All specimens were prepared by putting pieces of full-thickness skin approximately 1 cm. square into a cold-sterilized Stadie-Riggs microtome[27] and slicing off, parallel to the surface of the skin, a top layer less than 0.5 mm. thick, which consists of the epidermis and a thin layer of dermis. This sheet of viable skin was immediately placed on the appropriate medium, taking care that the dermal side was down and that the specimen was flat and completely in contact with the substrate.

Both liquid and agar media were used. The liquid media were contained in a microculture slide with a straight-wall concavity of 0.5 ml. capacity. When

full, a small square of lens paper covered the opening and was in contact with the fluid without air bubbles. The lens paper was treated in three ether, three absolute alcohol, and five distilled water washes for one hour each before autoclaving and positioning. The thin sheet of skin was placed on the paper, made translucent by the underlying fluid, but care was taken to prevent a pool of medium forming around the skin. The slides were incubated in covered sterile Petri dishes.

The agar media were made by adding appropriate solutions and sera to 4% agar in distilled water that had been melted by heating but was cooled to 45 C as the other ingredients were added. The media containing a final 1% agar were poured into small (60 mm.) Petri dishes, and the skin was positioned on the surface after the agar had hardened.

The media used varied in different experiments. The diluent throughout, however, was Hank's balanced salt solution. Concentrations were planned so that the final dilutions resulted in the usual concentration of salts plus 1.0% glucose and neomycin, 250μg. per milliliter, and bacitracin, 100 units per milliliter. Instead of bicarbonate, tris (hydroxymethyl aminomethane), 2.0 mg. per milliliter, was used as the buffer, as described by Swim and Parker.[28] The pH was approximately 7.2-7.4. Incubation was at 35 C, as being nearer normal skin temperature than the usual 37 C. In the incubator the agar or the slide-containing Petri dishes were stacked in the copper cans used for this purpose, with the openings closed to reduce evaporation. In some experiments the skin sheets were moved to fresh slides or to new areas of agar at varying intervals without difficulty.

The fungi used to inoculate the skin were in the form of tiny pellets, similar to those described by Raubitschek.[29] One of the pellets was put in the center of the planted skin after the skin had been in place and incubated for two hours. The pellets were prepared by inoculating flasks containing Sabouraud's broth plus 0.5% yeast extract with material from fresh slants of Trichophyton rubrum or Trichophyton mentagrophytes. After one week of incubation at room temperature on a gyrorotary shaker, the pellets were removed and stored in a refrigerator to be used within several days.

After suitable incubation the skin was removed from the agar or paper and fixed in chromic acid Bouin's solution. Paraffin sections were stained with various combinations of the periodic acid-Schiff stain plus hematoxylin plus metanil yellow. Usually all three were used on the same slide, and this combination, which is essentially the "Gridley fungus stain," is to be recommended because it shows not only the fungal elements but also good nuclear and cell detail.

Results

More than 500 pieces of skin have been grown on a wide range of media and by many techniques. As Blank et. al.[4] had demonstrated earlier on the chick embryo chorioallantois, the prepuce provides a particularly useful source of human skin for organ culture, but skin from adults will also grow with ease. In histologic sections of cultured skin it is immediately apparent whether the tissue is alive or not (Fig. 3). Dead cells do not take the stains, especially hematoxylin; the nuclei are pyknotic, degenerated, or absent, and the general archi-

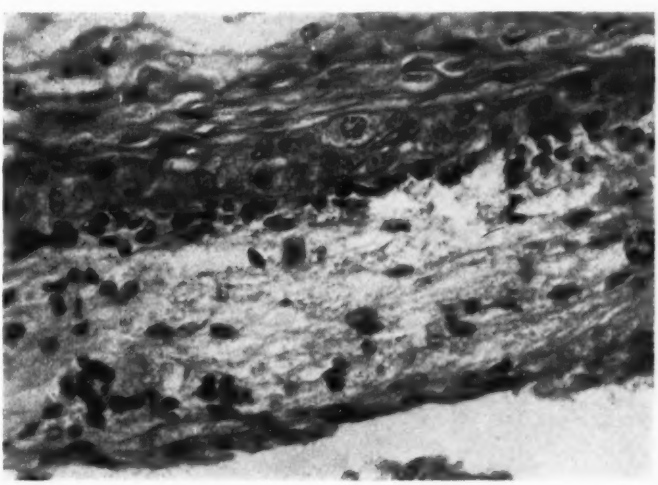

Fig. 3. — Section of human prepuce after growing on agar medium (changed three times a week) for 21 days. The looser dermis is easily distinguished from the epidermis, which contains a mitotic figure.

tecture, including cell outlines, becomes indistinct (Fig. 9). In our studies it was unusual to find skin which did not grow well. Frequently, however, certain areas in a piece would do better than others. It was common for the stratum mucosum, usually the outermost layers, to degenerate, but almost invariably a new stratified epidermis promptly re-formed under it. Dermal elements, including fibroblasts, blood vessels, and the epidermal appendages, seem to survive. The sweat glands grow particularly well. Mitoses could be found in varying numbers in the epidermis even after four weeks of continuous culture in vitro. Because of the particular problem under investigation, most tissues were fixed after 48 or 72 hours, but the technique can be recommended for longer periods, moving the skin to fresh media at 48- or 72-hour intervals.

When the pellets of fungi, which consist of a round mass of mycelia, are planted directly onto Sabouraud's agar they grow rapidly, spreading over the surface and into the medium, as reported by Lewis and Hopper[18] (Fig. 1*A*). On a nutrient agar containing 50% or more of serum, the pellets remain stationary, and only slowly begin to grow after several days, in spite of the large size of the mycelial inoculum and the presence of necessary nutrients (Fig. 1*B*).

To determine the potential for growth of fungi present in a typical clinical lesion of tinea, thin sheets of surgically removed pieces of infected skin were planted on the surface of Sabouraud's agar. The sparse mycelia, limited to the stratum corneum in the specimen fixed at the time of biopsy (Fig. 4), is in sharp contrast to the profuse fungal growth, with invasion of epidermis and dermis, which occurs after 48 hours' incubation outside of the body (Fig. 5). These results were found consistently. It was noticed that the skin seemed to do surprisingly well growing on ordinary Sabouraud's agar, especially the epidermis nearest the profuse fungal growth. Although there was some suggestion of acantholysis of the epithelial cells, possibly from proteolytic enzyme action, as reported by Cruickshank and Trotter,[7] the epidermal cells with their nuclei are viable and undergo multiplication, as indicated by the mitosis in Figure 6.

To produce experimental infections of the cultured skin, the tiny pellets of fungi, as described above, were especially useful. They permitted an initial infection, limited to the center of the surface of the piece of skin without danger of immediate contamination of the sides or undersurface of the tissue, as might occur with a liquid inoculum of suspended fungal elements. In

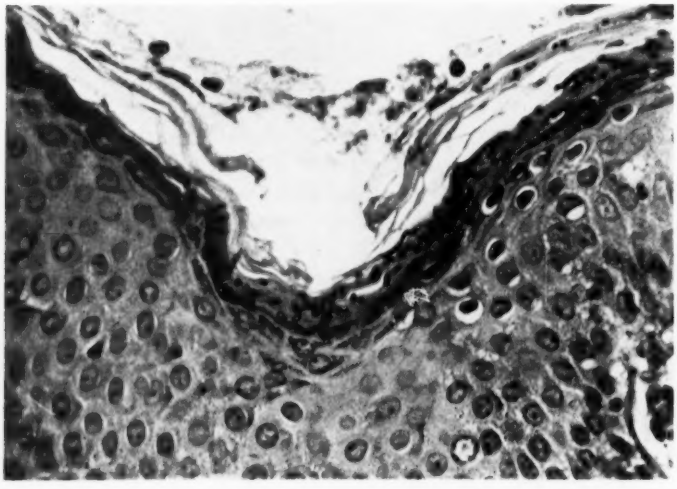

Fig. 4.—Biopsy specimen of tinea circinata caused by T. rubrum. The mycelia characteristically are limited to the stratum corneum.

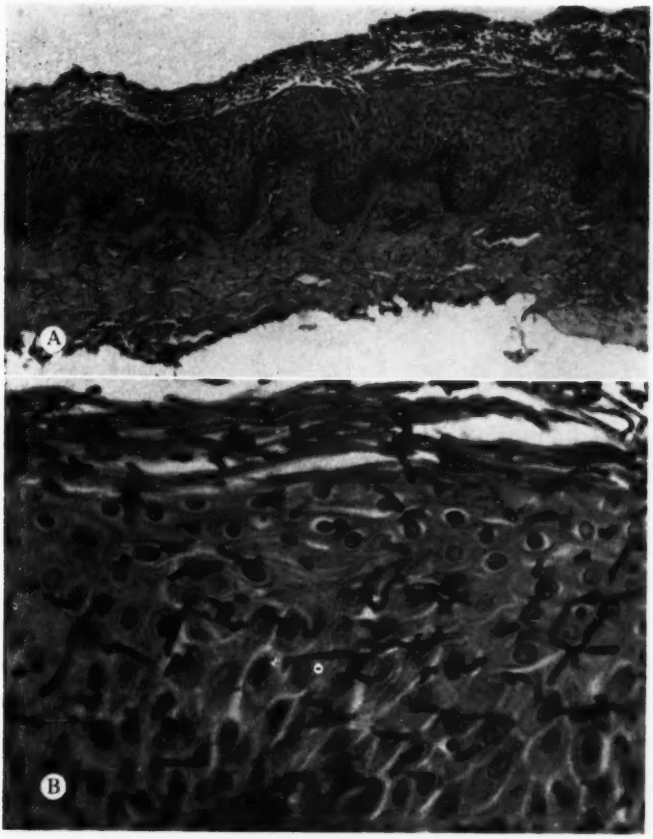

Fig. 5.—*A*, section of same tissue as in Figure 1, but fixed after 96 hours' incubation on Sabouraud's agar. The mycelia have multiplied profusely, invading the living epidermis and dermis. *B*, high-power view of *A*, showing epithelial invasion.

the experiments to study the role of serum factors in cutaneous fungal growth it was found that 48 hours' incubation was optimum. Easily recognized invasion occurs in two days, but longer periods of growth tend to obscure the effects. The inhibition, as

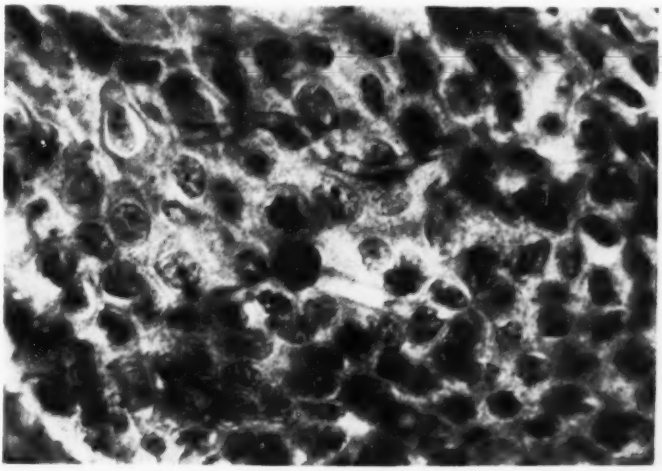

Fig. 6.—Oil-immersion view of histologic section of tissue, prepared as in Figure 5 but incubated only 48 hours on Sabouraud's agar. The mycelia above and below the mitotic figure illustrate active invasion of living epithelium by T. rubrum.

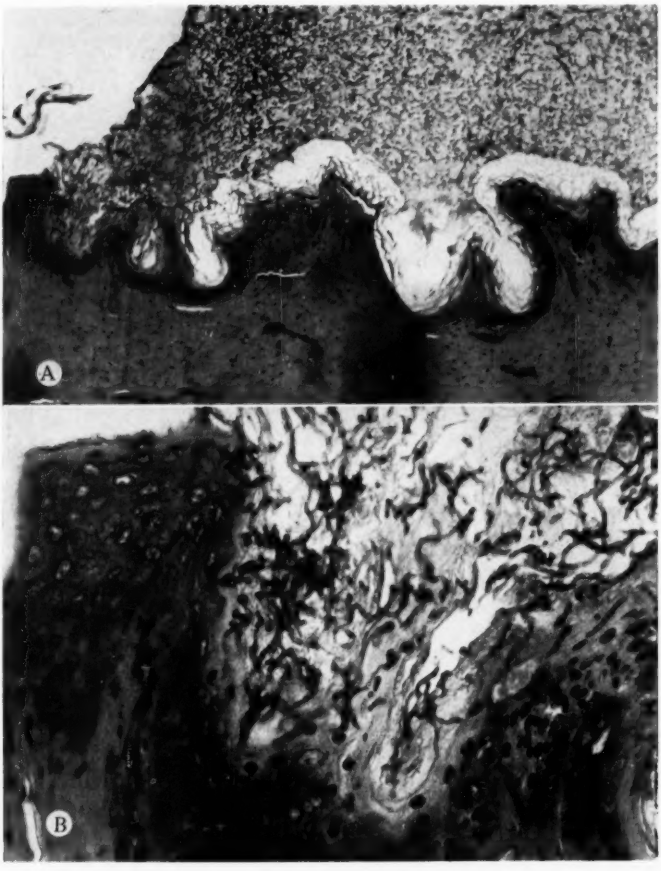

Fig. 7.—*A*, section of skin with fungal pellet inoculum (T. rubrum) after 48 hours' incubation on human serum medium. The mycelia have spread through the stratum corneum but have not invaded deeper. *B*, higher-power view of edge of *A*, showing mycelial growth which is practically indistinguishable at this site from natural human infection.

Results of Experiments

	T. Mentagrophytes Invasion of			T. Rubrum Invasion of		
	Stratum Corneum & Dead Epidermis	Living Epidermis	Dermis	Stratum Corneum & Dead Epidermis	Living Epidermis	Dermis
Serum						
100%	+++	0	0	+++	±	0
50%	+++	+	0	+++	++	0
25%	+++	++	+	+++	++	++
Dialized serum						
100%	+++	+	±	+++	++	+
50%	+++	++	++			
Heated serum						
100%	+++	+	+	+++	++	++
50%	+++	++	++			
Albumin, 5%	+++	++	++			
γ-Globulin, 5%	+++	++	++			
Fibrhgen, 5%	+++	++	++			
Fractions II & III, 5%	+++	++	++			
Fraction IV, 5%	+++	++	++			

Fig. 8.—Similar preparation as in Figure 7, but the fungal species is T. mentagrophytes. The granules in the epidermis are periodic acid-Schiff (PAS)-positive glycogen.

Lorincz et al.[19] found in their experiments, is fungistatic, not fungicidal, and eventually with continued incubation the large inocula grow out.

The growth of the dermatophytes was determined microscopically by examination of multiple histologic sections taken through the pellet and underlying skin. Usually the results were recorded without knowledge of the experimental protocol to minimize human bias. The sections were read independently by two observers. With a little experience the depth of invasion could be determined with accuracy. It was soon found that the mycelia at the periphery of the pellet had the greatest capacity to invade, and these areas were especially scrutinized in every section (about 10) on every slide. To record the results it was found convenient to establish arbitrary degrees of invasion. Only one mycelium found invading was indicated by ±; several, by +; moderate number, by ++; profuse, by +++. The results of many experiments are summarized in the Table. All experiments were performed in duplicate and were repeated at different times. Some materials, such as the effect of 100% normal human serum on invasion by T. mentagrophytes, were tested eight different

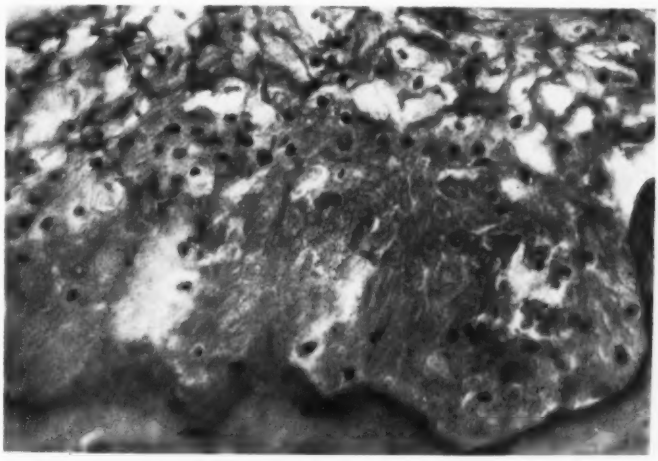

Fig. 9.—Section of biopsy specimen of tinea circinata caused by T. rubrum, incubated on 100% human serum for 48 hours. Photo taken in an area of necrotic epithelium. Mycelial proliferation is evident at the top, but invasion of the epithelium by fungus has been retarded.

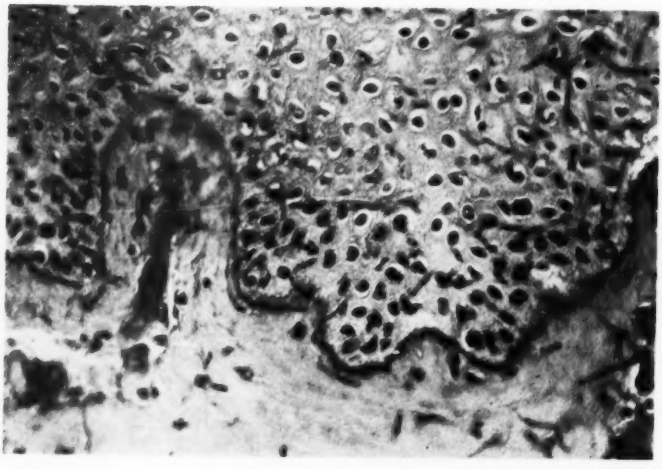

Fig. 10. — Section of tissue prepared as in Figure 9 but grown on liquid medium containing purified serum fractions: albumin, 3%, II and III, 1%, IV, 1%. Rapid invasion of living epithelium and dermis by mycelia is evident.

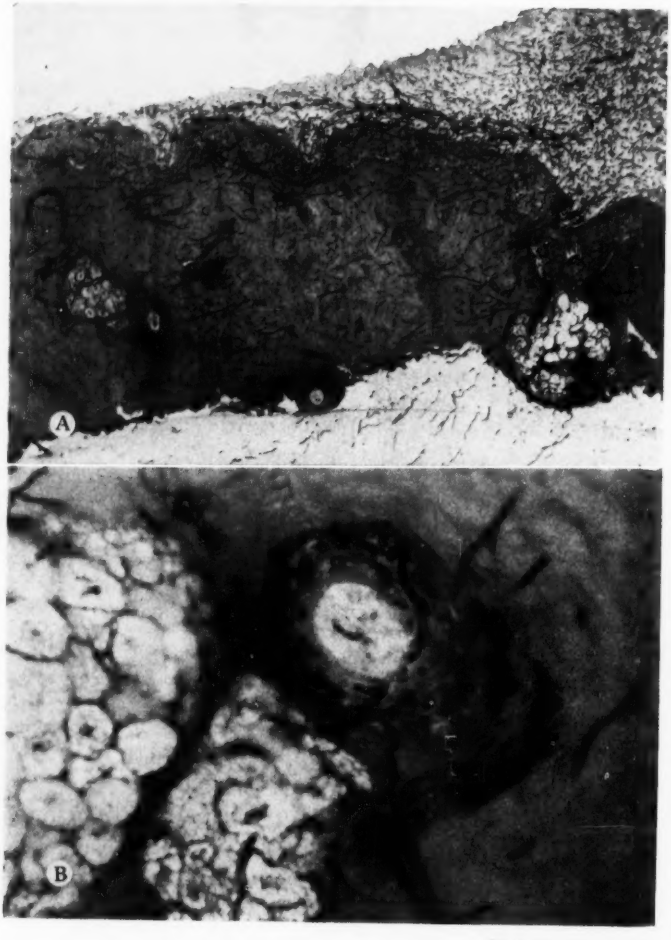

Fig. 11. — *A*, similar preparation as in Figures 7 and 8, but 5% γ-globulin has replaced the human serum in the agar medium. There is marked invasion of all layers of epidermis and dermis by the mycelia. *B*, high-power view of mycelia invading sebaceous gland and hair follicle in dermis of *A*. (Sebaceous glands and lanugo hairs are surprisingly common in the preputial skin.)

times over a period of many months to be certain that the results were consistent and reliable.

These experiments appear to have demonstrated that dermatophytes are prevented from invading the living epidermis and dermis by the fungistatic effect of normal serum (Figs. 7, 8, and 9). Decreasing concentrations of the serum permit deeper invasion. Of interest was the greater invasiveness of T. rubrum, as compared with T. mentagrophytes, for the same situation obtains in the living host (Wilson et al.[30]). Silva suggests that it may result from the greater tolerance of T. rubrum for hydroxyproline.[25] It contrasts with the report of Ajello and Georg[2] that hair suspended in water will be invaded by T. mentagrophytes but not by T. rubrum. Although theirs is a valuable test for identification, it does not simulate the usual host-parasite relationship.

In an attempt to gain information on the nature of the fungistatic material, sera were tested after dialysis against the Hank's solution as described and also after heating to 56 C in a water bath for 30 minutes. Both procedures reduced the fungistatic effect, but neither destroyed it completely. Protein fractions, including γ-globulin, serum albumin, Cohen Fractions II, III, and IV, and fibrinogen, were each tested in a 5% concentration in Hank's solution and in combinations but showed no inhibitory activity. (Figs. 10 and 11 provide additional examples of typical invasion in the absence of the inhibitory serum factor.)

Comment

In recent years a number of investigators have produced evidence throwing doubt on the concept of keratinophilia of dermatophytes in the sense that they grow in this material by their own selection or metabolic choice. The idea that they are necrophilic and will multiply only in dead tissue also has been contested and defended.[16] From our studies, which are summarized in this report, it seems evident that both of these terms are probably misleading. The Greek *philein* means "to love." The dermatophytes do not "love" keratin or dead tissue, rather it seems that they can multiply only in such tissues where they are out of the reach of the inhibitory substances normally present in serum and presumably also in all intact living moist tissues.

We would heartily endorse Wilson's[29] thesis that further study of the host factors is likely to be a very rewarding direction of mycologic research. By manipulating the tissue milieu in which the fungi grow it may become possible to understand and affect the factors which result in clinical resistance and susceptibility to disease.

Some progress is being made in similar studies with bacterial infections. Ho and Kass have reported recently a protective activity in normal sera against bacterial endotoxins.[9] Their factor, which seemed to be an enzyme, was found in Fractions II and III, in contrast to the antidermatophyte activity which is absent in these prepared fractions. The existence of multiple natural protective factors in serum is illustrated further by our studies, being reported elsewhere, which suggest that the serum antifungal effect against dermatophyte fungi and the yeast Candida albicans are not identical.[23]

Summary

Human skin, both newborn and adult, can be grown with ease as an organized tissue on the surface of agar media or on lens-paper-covered liquid media.

Infection of such skin with the dermatophytes, Trichophyton mentagrophytes or Trichophyton rubrum, simulates natural human infection.

The precise localization of dermatophytic infections to dead outer keratinized structures in a living host apparently results from the fungistatic effect of serum.

The superficial fungi are unable to invade living tissue if it contains the factors present in normal human serum. If the serum factors are absent, however, the mycelia readily invade all layers and structures of living skin.

The substances which produce fungistasis are not yet known. Neither γ-globulin nor other protein fractions, such as albumin and Fractions II and III or IV, seem to possess such activity.

Dialysis and heating (56 C) diminish the antifungal activity of serum when tested in infected organ cultures.

The grant of the Council on Drugs of the American Medical Association aided in the purchase of a microtome; Dr. Frank H. Clarke, of Lederle Laboratories Division, American Cyanamid Company, and Dr. Benjamin E. Sanders, of Merck Sharpe & Dohme, furnished protein fractions.

University of Miami School of Medicine, Jackson Memorial Hospital (36).

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The Treatment of Pruritus in Hodgkin's Disease with Demecolcine (Colcemid)

Report of a Case

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Pruritus is a well-recognized manifestation of Hodgkin's disease. It is present in about 20% [1] of the cases and usually follows the clearer evidences of this disease but may antedate by a considerable time the characteristic lymphoid changes.[2] The itching is generalized and intensified during the patient's fitful sleep. The character, distribution, and amount of excoriation can resemble heavy ectoparasitic infestation. The cause of the pruritus is unknown, and it is assumed to be the effect of a general "toxic" state resulting from active and usually extensive Hodgkin's disease. X-ray irradiation of the active foci or the use of cytotoxic substances is the most effective therapeutic measure available.

At a panel discussion on Hodgkin's disease at the New England Deaconess Hospital, in Boston, in the spring of 1958, Dr. Edmund W. Campbell, of the Lahey Clinic, one of the panelists, suggested the use of demecolcine (Colcemid) in the treatment of refractory Hodgkin's pruritus. In a review of the available literature, we were unable to find any reports on the use of this drug in the pruritus of Hodgkin's disease. Holly et al.[3] report the use of this drug in 10 patients with Hodgkin's disease, with prompt temporary regression of the disease but with rapid development of resistance.

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The opinions or assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

In 1950, Santavý and Reichstein, cited by Uffer et al.,[4] reported the isolation of several previously unknown alkaloids from the bulb of meadow saffron (Colchicum autumnale), the source of colchicine. Colcemid, which is a Ciba pharmaceutical product, is one of these natural crystalline alkaloids and differs structurally from colchicine in that a methyl group replaces an acetyl group at the N-position. In spite of its relative freedom from gastrointestinal side-reactions and its being 30 times less toxic than colchicine, it is not available for use in acute gout as a substitute for colchicine because of its potentially more serious toxic effects.[5] Demecolcine is a potent antimitotic agent, arresting mitosis in the metaphase. Although pancytopenia may occur,[5] it has a unique selective inhibition of granulocytic production, and often there is an associated thrombocytosis. This drug is a useful addition for the treatment of chronic myeloid leukemia.[6] The remission induced may be prolonged if the patient receives a maintenance dose. Shanbrom and Kahn [7] reported the resolution of cutaneous nodules of chronic myelogenous and acute monocytic leukemia with demecolcine. This drug may be administered orally or intravenously.[8,9] The dosage is not well established but ranges between 1.0 mg. and 15.0 mg.; an average dose is 5 mg. The toxic side-reactions are nausea, vomiting, diarrhea, pruritus,[8] maculopapular eruption,[10] alopecia,[8,11] inhibition of spermatogenesis,[12,13] and agranulocytosis [13] with or without secondary upper respiratory tract ulcerations. These effects are transient and disappear with the cessation of the drug.

We wish to present a case of Hodgkin's disease with severe pruritus which responded dramatically to demecolcine, which had to be discontinued because of severe agranulocytosis.

Report of Case

The patient is a 28-year-old white woman who 10 years ago noted a swelling on her anterior chest wall. This swelling was biopsied, and the pathology report was Hodgkin's disease. The lesion responded to x-ray therapy. She subsequently developed axillary, cervical, and hilar lymphadenopathy as well as multiple costal and sternal involvement. From 1949 to 1951 she had one course of mechlorethamine hydrochloride (nitrogen mustard) (24 mg. over five days) and innumerable courses of x-ray to various active foci of disease.

In February, 1951, she had herpes zoster of her right forearm. These lesions healed, leaving raised, bluish, nonpruritic nodules. Because of their persistence, one of these lesions was biopsied in September, 1951, and it was reported by several pathologists as consistent with Hodgkin's granuloma of the skin. The area was treated with the cathode ray at the Massachusetts Institute of Technology. At this time she was also treated with supervoltage x-ray to the neck and mediastinal nodes.

Until May, 1956, her disease was relatively quiescent. However, for the first time, she complained of pruritus, which was localized mostly in the previously irradiated sites. She was given tripelennamine (Pyribenzamine), with no relief. In July, 1956, she had a gradual swelling of her left upper arm, which measured 3 in. greater in circumference than her right upper arm. There was no clinical evidence of an underlying circulatory disturbance. In November, 1956, an examining physician described her present generalized dusky pigmentation.

In December, 1956, she had a flare-up of her disease, which was characterized by malaise, increased pruritus, lymphadenopathy, and increased swelling of her left arm. The relief she experienced from a course of mechlorethamine hydrochloride (40 mg. in four equally divided injections) lasted only six weeks. She was then given a course of TEM (total, 35 mg.), which gave her some symptomatic relief and did reduce temporarily her lymphadenopathy. The dimenhydrinate (Dramamine) she received for nausea had no appreciable effect on the intensity of her pruritus. In May and June, 1957, she received more x-ray therapy to her enlarged nodes. In spite of the above local therapy and more, her clinical course was characterized by temporary incomplete remissions with recurrences of equal or greater intensity.

By January, 1958, the itching was so severe that the patient was exhausted from continuous scratching and sleeplessness. Her entire body was covered with excoriations. She was admitted to the U. S. Naval Hospital, Chelsea, Mass. She experienced no relief of her pruritus with medicated baths and lotions, chlorpheniramine (Chlor-Trimeton), and perphenazine (Trilafon). The patient experienced some relief of her pruritus with a course of triamcinolone (Aristocort) (35 mg. daily P. O. for six weeks) and repository corticotropin injection (Acthar-Gel) for one week but developed marked Cushingoid features. Upon the discontinuance of the above steroid therapy, the pruritus again became almost intolerable. A trial of thenalidine (Sandostene) did not affect her itching.

In April, 1958, she was readmitted to the U. S. Naval Hospital because of fever and pruritus. She was given 40 mg. of mechlorethamine hydrochloride in divided doses. Her fever subsided, and her pruritus was less. She was given chlorpromazine (Thorazine) which relieved her nausea but had no noticeable effect on the intensity of her pruritus.

On July 15, she was seen in the outpatient clinic because of anorexia, weight loss (20 lbs. in eight weeks), weakness, fatigue, severe pruritus, and lymphadenopathy. On physical examination the patient presented a generalized dusky pigmentation of the skin with much excoriation and superficial scarring. There were no areas of cutaneous infiltration. The cervical, axillary, and, for the first time, inguinal lymph nodes were enlarged. There was no hepatosplenomegaly. The left upper arm was 6 in. larger in circumference than the right. The remainder of the physical examination was not remarkable. The white blood cell count was 6,800, with a normal differential. The hemoglobin was 9.5 gm., and a hematocrit, 32 vol. %. The C-reactive protein was 3+ (range is negative to 4+). The x-ray of the chest revealed a minimal widening of the superior mediastinum, which had been described for the past two years. In view of the relative severity of her disease, especially the pruritus which had been hitherto almost refractory to all therapy, demecolcine was administered orally. Over a period of 14 days, she received a total of 71 mg. Demecolcine was begun on July 18, when she was given 1 mg. four times a day. After one week, she had taken a total of 28 mg., with no change in her clinical status and no manifestations of drug toxicity. Her white blood cell count was 6,350, with a normal differential. On July 25, the dose was increased to 6 mg. daily. On July 26, she was anorexic and nauseated. On July 28, she suddenly experienced a diffuse and marked defluvium of the hair of her scalp. On July 30, she experienced a sore mouth, fever, and chills. She noted also at this time the sudden and almost complete relief of her itching.

On Aug. 1, she was readmitted because of continued fever and chills, generalized malaise, sore throat, and tender, submaxillary nodes. Her white blood cell count was 400, with 14% neutrophils and 86% lymphocytes; her hemoglobin was 9 gm., and her hematocrit was 27 vol. %. The urine contained 20 mg. % of albumin. Two sternal marrow aspirations were unsuccessful. Demecolcine therapy was discontinued. She was immediately given heavy antibiotic coverage with penicillin, chloramphenicol (Chloromycetin), and erythromycin in maximal dosages, and supportive transfusions. On Aug. 3, the white blood cell count fell to 150, and only two lymphocytes were noted in the peripheral smear. On Aug. 6, the white blood cell count was 300 and the patient was started on high doses of prednisone (Meticorten) (80 mg. daily). Within the next 10 days, the white blood cell count rose to 5,400, with a normal differential. The C-reactive protein was reported as negative at this time. The antibiotics were discontinued, and the prednisone was gradually being diminished when, on Aug. 23, the patient developed a severe gastrointestinal hemorrhage. The site of hemorrhage was not detectable by x-ray study. She improved with blood transfusions and a peptic ulcer regime. On Aug. 28, about four weeks after cessation of demecolcine therapy, the patient noted the absence of further hair loss.

At seven weeks after the discontinuance of demecolcine therapy, the patient was completely free of her pruritus; the lymphadenopathy was greatly reduced, and the upper left arm had become 4 in. smaller in circumference. She felt symptomatically "the best in years." There was no change in the degree of her scalp hair loss, an estimated 50%, and no evidence of regrowth at this time.

Comment

In an attempt to relieve her pruritus, the patient received medicated baths and lotions, tripelennamine, dimenhydrinate, chlorpheniramine, thenalidine, chlorpromazine, perphenazine (Trilafon), triamcinolone, and repository corticotropin injection. One course of TEM and two courses of mechlorethamine hydrochloride were given within a period of 20 months, and each course was followed by a temporary diminution in the intensity of the pruritus. For the past two years, in spite of the above therapeutic measures, pruritus has remained at all times the leading symptom. Therefore, its sudden and complete relief with demecolcine was dramatic. It occurred on the 13th day of therapy when the dose had totaled 64 mg. and while she was experiencing the toxic symptoms of nausea, vomiting, and alopecia. The patient has remained free of her pruritus up to the time of the submission of this article for publication (seven weeks).

The over-all improvement of our patient's physical status following the use of demecolcine is impressive; however, a longer period of observation is warranted before attempting any conclusions. One must also remember that Hodgkin's disease can undergo spontaneous remission. Of possible significance was the change of the C-reactive protein from 3+ to negative at the conclusion of therapy.[14]

On review of the literature and the above case, one is impressed by the potentially severe toxicity of this drug. Like Mikkelsen et al.,[11] we were unable to find reports of maximum safe dosage in patients with normal rather than hyperplastic marrows. Bock and Gross[15] reported four cases of Hodgkin's granulomas treated with demecolcine. Two of them showed some regression in the size of lymph nodes, one, after 211 mg. of demecolcine was given over 29 days and the other after 114 mg. was given over 16 days. In the other two cases, the medication had to be stopped because of granulocytopenia. Zbinden,[16] in the discussion of the use of demecolcine in Hodgkin's disease, concluded that the risk encountered in using this drug in high dosage did not sensibly compare to the effect on the course of the disease. Moeschlin et al.[12] warn against its use in neoplasms, such as myeloma, lymphosarcoma, Hodgkin's disease, carcinoma, and sarcoma, because they observed deaths attributable to agranulocytosis. One of these patients received a total dose of 65 mg. in 13 days. Because of the chronicity and intensity of our patient's pruritus, with its incumbent severe physical and mental effects, we felt justified in the use of this drug. When she developed fever, chills, and ulcerative pharyngitis, complete blood cell counts revealed agranulocytosis. She was treated, as were the

The amount of alopecia the patient exhibited three weeks after the cessation of demecolcine therapy.

cases of Sheehy and Ransone,[17] with multiple antibiotics, steroids, and supportive blood transfusions. The hematologic toxicity can be severe enough to resemble leukopenic leukemia.[18]

During the second week of therapy with demecolcine the patient experienced a sudden and diffuse defluvium of scalp hair, and this process continued very slowly for the next four weeks. She lost about 50% of her scalp hair. Alopecia is not an unusual toxic occurrence during or after therapy. Colsky et al.[5] report a case who not only experienced loss of scalp hair but also absence of beard growth and sparcity of eyebrows and body hair. Piney[19] reports a patient with chronic myeloid leukemia who, after four months of 15 mg. daily, developed a remarkable loss of hair, which regrew in spite of continued big doses. The regrowth of hair usually occurs in three to four months after the cessation of therapy. Wildhack[20] biopsied the skin of the scalp of three patients who developed alopecia from demecolcine and concluded that the depilation is due to defective cell regeneration.

There are several interesting medical and dermatologic facets to this case. The peculiar generalized dusky pigmentation present for two years in this patient is consistent with the report of pigmentation as a possible cutaneous manifestation of an underlying Hodgkin's disease.[21] The diffuse swelling of the left shoulder and upper arm still remains unexplained. A biopsy was not done, but for two years it was assumed that this swelling represented lymphedema which resulted secondarily from x-ray irradiation of the axillary area. The dramatic reduction in size of this swelling after administration of demecolcine was surprising and raises the question whether this swelling could represent a diffuse muscular infiltration by Hodgkin's disease which responded to demecolcine. The prompt and complete response of the cutaneous nodules of Hodgkin's disease to the cathode ray was very gratifying. The patient called our attention to the healed sites of three verrucae

vulgaris, which disappeared during demecolcine therapy.

One gains the impression from this case and others reported in the literature [5,8,11,18] that dosage as well as individual idiosyncrasy are the determining factors in the incidence of the toxic effects and that patients experiencing severe marrow depression are more apt to have an associated alopecia.

Summary

A case of Hodgkin's disease of 10 years' duration with generalized pruritus of the skin of 2 years' duration is presented.

Demecolcine (Colcemid) dramatically and completely relieved the pruritus, which was previously resistant to all other forms of therapy.

Unfortunately, the patient experienced toxic reactions to demecolcine, characterized by gastrointestinal symptoms, alopecia, and a severe agranulocytosis, which necessitated interruption of therapy.

Addendum

The remission lasted nine weeks, after which time there was complete regrowth of hair. The recurrence was characterized by generalized pruritus, fever, asthenia, and marked inguinal and retroperitoneal lymphadenopathy. An attempt to control the patient's pruritus with high doses of trimeprazine (Temaril) failed. The disease was refractory to x-ray therapy (both conventional and supervoltage) to involved areas and mechlorethamine hydrochloride (nitrogen mustard), and the patient died seven months after the completion of demecolcine (Colcemid) therapy. At autopsy there was widespread Hodgkin's disease, involving the entire lymphatic system except liver and spleen, with direct extension into pleura, lungs, bones, and adrenal and thyroid glands. The left biceps, triceps, and pectoral muscles were replaced by tumor tissue.

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Neurilemmoma of the Tongue

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A neurilemmoma or Schwann cell tumor is a distinctive nerve sheath tumor, characterized histologically by the regimentation of its cells. It is probably seen more commonly by surgeons than by dermatologists. While dermatology texts refer to it, no original article was found in the American dermatologic literature of the past 20 years. The following is a synopsis of statements found in several books.[1-10]

Neurilemmomas usually are solitary and affect women more frequently than men in a mean ratio of about 7:4,[11,12] without particular affinity for any age group. They occur commonly on the cranial nerves (except the olfactory and optic), with the acoustic nerve being the one most frequently affected in its vestibular branch. When peripheral neurilemmomas are found, they are seen to occur on nerves in the scalp, face, sides of the neck, tongue, flexures of the arms, wrists, knees and ankles, wall of the stomach, intestines and aorta, and rarely on the trunk.[11] A relatively frequent site is the posterior mediastinum,[13] and it apparently occurs only on very rare occasions within bone.[14] In a minority of cases, the tumors are multiple or are accompanied by neurofibromatosis,[15] hence the finding of one neurilemmoma should lead to a careful examination of nerves elsewhere on the body, even though this will prove fruitless in most cases.

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The lesions are slow-growing, well-circumscribed, and essentially benign, although it has been stated that a neurosarcoma represents the malignant transformation of a neurilemmoma or neurofibroma. Allen[7] believes that the few malignant neurilemmomas which have been observed appear to have been cancerous from their beginning rather than to have evolved from a benign schwannoma.

Tumors may range in size from several millimeters to several centimeters when they occur superficially and grow much larger in visceral regions. They are rounded or ovoid, with a uniform texture and with consistency varying from soft to moderately firm. When they are soft and fluctuant, this usually signifies cystic degeneration. The color may be pink, gray, or yellowish, and small intradermal tumors resemble nevi. Occasionally the surface displays hemorrhagic foci, and telangiectasia is frequently seen at the periphery of degenerating neurilemmomas which are occasionally misjudged as hemangiomatous tumors. The diagnosis is often suspected when the lesions are associated with pain, especially if this is of the paroxysmal type.[16] Clinically neurilemmomas may simulate a lipoma, carotid body tumor, or salivary gland tumor, a metastasis, an epidermal or sebaceous cyst, a synovial ganglion, a juxta-articular node, a hygroma, a hemangioma, a neurinoma, and a neurofibroma or neurofibrosarcoma.

Histologically, the orderly arrangement of parallel cells, separated by aggregations of collagenous fibers, gives the aforementioned regimentation, or palisade pattern. Anderson[3] has excellently described it as "an interlacing network of wavy, flowing streams of cells in which the nuclei palisade

prominently." The cells resemble those of Schwann, and the above pattern mimics the neurilemmal supporting elements of Meissner's tactile corpuscles.[16] This is known as Antoni Type A tissue, while Type B shows no orientation of cells and fibers but intercellular fluid, which, when collected, may result in microcystic degeneration. Type B is considered to be a degenerative condition of Type A. Both types may occur in the same tumor in varying amounts. Occasionally the cells may be less regularly arranged and more whorled,[17] and the nuclei may be seen to lie in a double palisade, enclosing a space nearly devoid of nuclei. This is a so-called Verocay body, named after its discoverer who first adequately described neurilemmomas, in 1908. There may be edematous foci or areas of microcytic degeneration in the tumor mass. Lipid histiocytes and hemosiderophages are commonly observed in and about the degenerated areas if such exist in the tumor. Mast cells are often present in conspicuous numbers. The tumor itself very rarely contains nerve fibers; these lie outside the capsule, and hence the name "neurinoma," which is frequently used for these lesions, is a misnomer.

As regards their pathogenesis, they are neoplasms which arise from the sheath of Schwann (Foot[17]) and do so spontaneously or possibly secondary to trauma or irritation of the involved nerve trunk.[11,18]

Complete surgical removal by excision is curative.

Report of a Case

The patient, a white man, 22 years of age, was first seen on May 12, 1958, with an ulceration on the right side of the tip of the tongue, which had been present for five days. The lesion was shallow, 2 mm. in diameter, slightly edematous, and tender and suggested an aphthous ulcer or herpes simplex infection. Two weeks later the patient returned, with a pink granulomatous-looking nodule on the tongue at the site of the previous ulceration. It was 1 cm. in diameter and raised 6 mm. from the surface of the tongue. The surface of the lesion itself was smooth, and it was firm and tender to the touch. The patient complained of intermittent pain in the area. There was no associated lymphadenopathy discernible; no other tumors were found elsewhere on the cutaneous surface, and the patient was in good general health. He stated that the previous ulceration had healed over a day or so after his first visit and soon thereafter the nodule he now presented had begun to make its appearance and grew slowly to its present size.

The lesion was excised in toto, and the gross specimen was almost mushroom-shaped, with a fairly broad but short stalk approximately 2 mm. long. The under-surface of the lesion revealed a number of small millet-sized and millet-shaped grains which were attached loosely by small strands. On seeing this gross specimen, one of us (C. M.) remarked that he had never seen this type of new growth previously.

The biopsy report by Dr. Hermann Pinkus was as follows:

"The lesion is composed of spindle-cells that are frequently arranged in palisaded fashion. Between the nuclear palisades there is a small amount of finely fibrillar tissue, which stains as connective tissue with the Van Gieson Stain. The tissue showing nuclear palisading is characteristic of Schwannian growth, which is best classified as a neurilemmoma. There is no evidence of malignancy.

Fig. 1.—Section stained with hematoxylin and eosin; × 28.

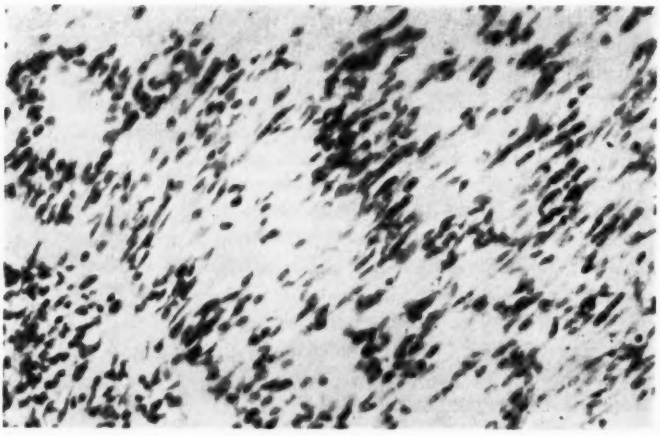

Fig. 2.—Similar section; × 280.

Diagnosis: Neurilemmoma of Tongue." (Figs. 1 and 2).

It is interesting to note in this case that trauma (in the form of local irritation by whatever cause) preceded the onset of the lesion by approximately one week and that the lesion itself grew to the size of a split pea in the period of 12 days or so.

Summary

A review of the clinical picture, histopathology, pathogenesis, and treatment of neurilemmoma is presented with report of a case in which it occurred on the tongue. No reports of neurilemmomas were found in the dermatologic literature during the past 20 years.

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The Cutaneous Reaction to Nicotinic Acid (Niacin)-Furfuryl

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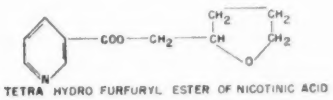
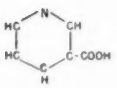
The purpose of this study was to observe the cutaneous reactions of nicotinic acid (niacin)-furfuryl in various disease states and to carry out clinical experiments related to the mechanism or mechanisms involved. There is considerable evidence, as will be shown, that a thorough knowledge of this subject might lead to a better understanding of the pathogenesis of atopic dermatitis.

The drug used in this study was the tetrahydrofurfuryl ester of nicotinic acid.



TETRA HYDRO FURFURYL ESTER OF NICOTINIC ACID



NICOTINIC ACID

Incorporated in an ointment it was first used as a rubefacient in inflammatory joint disease.

If a small amount of 5% nicotinic acid furfuryl in a hydrous wool fat (lanolin)-petrolatum base * is rubbed in or simply laid on the skin of normal persons and allowed to remain for 20 to 30 minutes, over 95% react with the production of erythema with or without edema. The reaction is termed "typical." It is also noted in a large number of different diseases, and because of this fact the term "normal" reaction cannot be used. The erythema produced disappears usually in from one to two hours.

Nassim and Banner [1] noted that when 5% nicotinic acid furfuryl ointment was applied to the skin of patients with active rheumatoid arthritis the typical reaction did not occur. Saslaw [2-4] found atypical reactions resulting from tests performed on children with acute rheumatic fever. The reaction consisted of a central area of non-edematous blanching surrounded by a slight amount of erythema. This response is one of temporary vasospasm. Similar results have been noted in untreated acute rheumatoid arthritis.[1,5] Saslaw stated that the reaction changed to a type, which he considered as a normal variant, as rheumatic activity decreased and as a result of steroid effect upon the reaction. Calloway noted that 5% nicotinic acid-furfuryl ointment applied to the involved areas of patients with atopic dermatitis caused a blanching or white reaction which was not found in testing patients with other types of cutaneous disease.[6]

A number of studies have been published relating to the specificity and mechanisms involved in the nicotinic acid-furfuryl test. Strehler believed that there is a histamine-like substance released in normal persons, but he was unable to block the hyperemia by local or internal use of antihistamines.[7] Weiss [8-10] studied the reaction in acute infectious disease and believes that atypical reactions result from the degree of constitutional stress imposed by the inflammatory disease and that this is an acute-phase reac-

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* The Trafuril Ointment used in this study was supplied by Ciba Pharmaceutical Products, Inc., Summit, N. J.

TABLE 1.—*Cutaneous Reaction to Nicotinic Acid-Furfuryl Ointment in Rheumatic Disease*

Diagnosis	Reaction				
	Blanching ± Peripheral Erythema	Nonreactive	Erythema ± Edema	Marked Blanched Edema ± Erythema	Total
Rheumatoid arthritis	18	0	9	0	27
Ankylosing spondylitis	2	0	0	0	2
Rheumatic fever	2	0	0	14 1 (?)	17

tion. He was able to accelerate the change from atypical to typical reactions in recovering patients by the administration of nicotinic acid. Haydu[11] published a study implicating Coenzymes I and II in this reaction and was able to alter results in normal persons and in patients with rheumatoid arthritis by topical application of an ointment containing diphosphopyridine nucleotide.

Method Routine Followed in Testing with Nicotinic Acid

Routine testing consisted of cleansing the test site with 70% ethyl alcohol, which was allowed to dry. Enough 5% nicotinic acid-furfuryl in a petrolatum base to cover 0.5 sq. cm. was gently applied to the skin and allowed to remain for 30 minutes, at which time it was gently removed with a cotton swab. A like amount of ointment base was used as a control near the test site. In patients with cutaneous disease, both substances were also applied to involved skin. Each patient was observed for 40 minutes, and, unless testing is done in groups, this is very time-consuming. Fifteen normal persons were initially tested, and the unpredictable amounts of erythema with or without edema, noted. It may be pointed out that the reaction should be observed in daylight, that delayed reactions may occur, and that the test is of no value in the Negro or other dark-skinned races.

Results

GROUP I.—Forty-six patients with rheumatic disease were tested. In this group were 27 patients with rheumatoid arthritis, 18 of whom revealed the atypical reaction manifested by central blanching with or without mild erythema. Two cases of ankylosing spondylitis revealed the same reaction, which is of some interest since there is considerable controversy regarding the question of whether rheumatoid spondylitis and peripheral rheumatoid arthritis are related diseases.

Seventeen cases of rheumatic fever were tested. Two of the group revealed atypical reactions and were the only cases we were able to obtain early in the course of their disease. The remaining 15 patients had been under therapy, including steroids, for at least three weeks, and testing with nicotinic acid-furfuryl revealed marked central blanched edema with peripheral erythematous flare. Edematous reactions are usually pale or pink, while these patients revealed a type of edema which was characterized by more pallor and had a yellowish tint. These cases were retested over a period of four weeks, and as they showed evidence of clinical improvement the peripheral flare became more extensive. This type of response was not noted by us in testing any other type of disease and is unclarified in the literature.

The relationship of drug therapy for rheumatoid arthritis to the cutaneous reaction to nicotinic acid-furfuryl ointment was significant. Of the 18 patients who revealed

TABLE 2.—*Relationship of Drug Therapy for Rheumatoid Arthritis to Cutaneous Reaction to Nicotinic Acid-Furfuryl Ointment*

Therapy	Reaction			
	Blanching ± Peripheral Erythema	Non-reactive	Erythema ± Edema	Total
Steroids	8	0	7	15
Acetylsalicylic acid	6	0	1	7
Butazolidin	2	0	0	2
Chloroquine	2	0	0	2
Gold	1	0	0	2

TABLE 3.—*Typical Reaction to Five per Cent Nicotinic Acid-Furfuryl Ointment in Various Types of Internal Disease*

Disease	Reactions, No.
Cardiovascular disease	2
Congestive heart failure	2
Coronary thrombosis	2
Pulmonary tuberculosis	10
Periarteritis nodosa	3
Bronchial asthma	1
Reiter's disease	2
Peptic ulcer	1
Acute nephritis	1
Simmonds disease	1
Whipples disease	1
Arthritis facticia	1
Degenerative joint disease	1
Gout	2
Total	30

atypical reactions, 8 were receiving steroids; 6, acetylsalicylic acid; 2, phenylbutazone (Butazolidin); 2, chloroquine, and 1, gold. This observation indicates that atypical reactivity is dependent upon the activity of the disease and is not altered by steroids or other drugs.

GROUP II.—Thirty patients with different types of internal disease were tested, including ten cases of active pulmonary tuberculosis. Each case responded with a typical reaction.

GROUP III.—Twenty-six patients with diabetes mellitus were tested.

TABLE 5.—*Typical Reactions Observed in Patients with Cutaneous Disease Tested with Five per Cent Nicotinic Acid-Furfuryl Ointment*

Disease	Reaction, No.
Vitiligo	1
Contact dermatitis	16
Carcinomatosis	2
Urticaria	2
Lichen chronicus simplex	1
Pemphigus	2
Erythema multiforme	1
Discoid lupus erythematosus	2
Basal-cell epithelioma	2
Polymorphic light eruption	1
Psoriasis	2
Lymphosarcoma	1
Lichen planus	1
Acne vulgaris	3
Total	37

TABLE 4.—*Cutaneous Reaction to Five per Cent Nicotinic Acid-Furfuryl Ointment in Twenty-Six Cases of Diabetes Mellitus*

	Reaction, No.		
Clinical Course	Blanching & Peripheral Erythema	Nonreactive	Erythema & Edema
Well controlled	0	0	13
Poorly controlled	0	5	8 (Very faint erythema)

It was noted that in 13 of the 26 cases tested, there was no reaction to nicotinic acid-furfuryl or a very slight or questionable amount of erythema was observed. Study of the nonreactive cases revealed that these patients were uncontrolled diabetics.

Nonreactivity in uncontrolled diabetes was the only unusual finding we encountered in testing patients with diseases unrelated to rheumatic or atopic disease.

GROUP IV.—Typical reactions were observed in 37 patients with various types of cutaneous disease, including 16 patients with contact dermatitis.

Fifteen patients with atopic dermatitis were observed. Thirteen cases showed blanching in involved skin, and two were nonreactive. Testing outside the involved areas showed typical or near-typical responses. Two cases of scleroderma were nonreactive. One of these patients was given an ample supply of 5% nicotinic acid-furfuryl ointment and instructed to massage the hands twice daily with the material. This was carried out for 8 weeks, and at no time did any reaction appear. There was subjective improvement in the scleroderma but inconclusive objective findings.

TABLE 6.—*Atypical Reactions in Patients with Cutaneous Disease Tested with Five per Cent Nicotinic Acid-Furfuryl Ointment*

Diagnosis	Cases No.	Reaction
Atopic dermatitis	15	Blanching in involved skin (13) Nonreactive in involved skin (2)
Scleroderma	2	Nonreactive
Total	17	

TABLE 7.—*Typical Reaction to Five per Cent Nicotinic Acid-Furfuryl Ointment in Neuropsychiatric States*

Condition	Reaction, No.
Schizophrenia	
Acute	1
Chronic	5
Simple	2
Catatonic	2
Paranoid	1
Anxiety, acute	1
Paraplegia (above and below cord injury)	12
Total	24

In a patient with atopic dermatitis, biopsies were performed on a blanched area after exposure to nicotinic acid-furfuryl and also on an area of uninvolved skin which showed a typical reaction. We were unable to make any significant observations. There were no eosinophils noted in the biopsy of the typical reaction.

GROUP V.—In view of the relationship of stress to activity in atopic dermatitis, 15 patients with mild to major psychiatric states were tested with 5% nicotinic acid-furfuryl ointment.

Results of this group were no different than would be expected in a similar group of normal patients.

Tweive paraplegic patients were tested, and no atypical reactions were noted above or below the site of cord injury.

Summary.—The testing of 183 cases with nicotinic acid-furfuryl revealed the following findings:

1. Patients with acute rheumatic disease during the period of early activity responded with an atypical reaction.

2. Patients with acute rheumatic fever during the first two months of recovery reveal a type of atypical reaction not noted elsewhere in this series.

3. Atypical blanching in patients with atopic dermatitis and nonreactivity in patients with scleroderma were the only significant findings in testing cutaneous disease.

4. No changes were noted in cases of mental disease or paraplegics which were different from normal patients.

5. With the exception of reactions described in cases of uncontrolled diabetics, nothing was learned by testing different types of internal disease, except as described above.

Experimental Studies Relating to Mode of Action of Nicotinic Acid-Furfuryl Ointment

GROUP I.—Seven patients were tested after iontophoresis with 2.5% tripelennamine (Pyribenzamine) hydrochloride in a water-soluble base at a selected site. The iontophoresis was carried out for 10 minutes at 2 ma., and a control blank plate was used. Application of nicotinic acid-furfuryl ointment at the site of tripelennamine iontophoresis revealed no different type of reaction from that noted at the site of the blank plate or at a control site.

GROUP II.—Seven patients recovering from acute rheumatic fever, who showed reactions to nicotinic acid-furfuryl manifested by central blanched edema and peripheral erythematous flare, were given 100 mg. of diphenhydramine (Benedryl) hydrochloride by mouth every 12 hours for 56 hours. Retesting after this period revealed a variable amount of reduction of the peripheral flare, compared with measured flare recorded in the controls, and this was not considered significant.

GROUP III.—Four institutionalized patients with diabetes mellitus were given 100 mg. of nicotinic

TABLE 8.—*Cutaneous Reaction to Five per Cent Nicotinic Acid-Furfuryl Ointment in Four Cases of Diabetes Mellitus Receiving Nicotinic Acid* *

Case No.	Reaction			Fasting Blood Sugar	
	Initial Test	Nicotinic Acid		18th Day	22d Day
1	Erythema, 1+	Erythema, 1+	Erythema, 1+; edema, 1+	185	212
2	Nonreactive	Erythema, faint	Erythema, faint	250	301
3	Erythema, 1+	Erythema, 1+; edema, faint	Erythema, 1+; edema, 1+	425	328
4	Erythema, faint	Erythema, faint	Erythema, 1+	93	105

* 300 mg./day; 2d, 3d, 5th, 11th, and 22d days.

TABLE 9.—*Effect of Inunction of Five per Cent Coenzyme I Ointment* *

Diagnosis	Cases, No.	Nicotinic Acid-Furfuryl After Inunction of Ointment Base		Nicotinic Acid-Furfuryl After Inunction of Coenzyme I	
		Reaction	No.	Reaction	No.
Rheumatoid arthritis	8	Nonreactive	4	No change	4
		Erythema, 1+	3	Increased erythema	4
		Erythema & edema	1		
Atopic dermatitis	2	Erythema & edema	1	No change	2
		Erythema	1		
Disseminated lupus erythematosus	1	Erythema, 1+	1	No change	1
Ankylosing spondylitis	1	Erythema, faint	1	Erythema, 1+	1

* Prior to tests with 5% nicotinic acid-furfuryl ointment.

acid by mouth three times daily, and cutaneous testing with nicotinic acid-furfuryl ointment was performed on the 2d, 3d, 5th, 11th, and 22d days of administration. Compared with the controls recorded prior to these tests, the changes brought about by the nicotinic acid appeared to be a slight altering of the reaction toward a more typical reaction.

GROUP IV.—In 12 patients, an ointment containing 5% diphosphopyridine nucleotide in a water-soluble base (Coenzyme I) was massaged into the skin with 30 strokes at moderate pressure per application. The material was allowed to penetrate for three minutes; excess ointment was removed and 5% nicotinic acid-furfuryl ointment applied to this site. Compared with the controls, no significant changes were noted after the routine hour of observation.

GROUP V.—In 13 patients an ointment containing 2.5% hydrocortisone and 5% nicotinic acid-furfuryl in a hydrous wool fat-petrolatum base was applied to selected sites and controls, and the base and the nicotinic acid-furfuryl were applied to adjacent skin. We were unable to see any difference between the steroid-nicotinic acid-furfuryl combination and in the nicotinic acid-furfuryl alone.

In five patients 2.5% hydrocortisone in a water-soluble base was massaged into the skin, and at the end of 10 minutes nicotinic acid-furfuryl ointment was applied to the same site. In none of these patients was any notable difference recorded, compared with the controls.

Comment

From results obtained by us from Groups I and II, it appears that there is no demonstrable relationship between histamine and the nicotinic acid-furfuryl reaction. These observations confirm the results of Strehler.

The administration of nicotinic acid to patients with diabetes mellitus in Group III, with resultant changes in the nicotinic acid-furfuryl reaction, may be of significance. It is known that patients with diabetes mellitus have an increased requirement for nicotinic acid, and Hallay [13] has reported that administration of nicotinic acid reduces insulin requirements. While Weiss has reported that nicotinic acid administration hastens the reappearance of typical from atypical reactions in cases of pneumonia, the direct result from the administration of this drug may be too simple an explanation of the mechanism involved. Further experiments with diabetics may prove worth while.

The experiment carried out with Group IV was based on the work of Haydu, who believes there is an increased requirement for adenosinetriphosphate in patients with rheumatoid arthritis. It follows that there would then be a deficiency also of Coenzyme I (diphosphopyridine nucleotide), with which adenosinetriphosphate is in dynamic equilibrium. Therefore, theoretically, when Coenzyme I is rubbed in, a more normal enzyme state is created, and atypical reactions to nicotinic acid-furfuryl would become typical reactions. This assumption is based on the belief that nicotinic acid-furfuryl produces erythema when combined with Coenzyme I. Haydu postulates that under normal conditions an excess of Coenzyme I applied to the skin places it in competition with normal tissue Coenzyme I and, therefore, typical reactions to nicotinic acid-furfuryl ointment are less apt to occur. The results obtained by us in 12 patients did not confirm the work published by Haydu. While the basis for implicating Coenzymes I and II with the nicotinic acid-furfuryl reaction may be theoretically sound, the fact remains that in no experiment to

our knowledge has the state of cutaneous blanching been reproduced by altering coenzyme concentrations.

So far as we were able to determine, local hydrocortisone does not affect the nicotinic acid-furfuryl reaction, as noted in Group V.

Observations which we have made in this study have convinced us that the nicotinic acid-furfuryl reaction is one of great interest and has the potential of leading to some fundamental knowledge of the biochemistry of certain diseases. We have been unable to explain the mechanism involved, and much laboratory investigation is needed. Experimental conditions necessary to allow vasodilatation as a result of exposure to nicotinic acid-furfuryl may have been accomplished; vasoconstriction has not been reproduced.

It appears evident that, while the reaction most frequently produces specific changes in patients with acute rheumatic disease and blanching in cases of atopy, the value of the test in these diseases is simply to add weight to a clinical and laboratory diagnosis with use of other means.

While there are many theoretical possibilities relating to the mechanisms involved in the nicotinic acid-furfuryl reaction, it is possible that serotonin may be involved. Asthma, flushing, migratory arthritis, and endocardial fibrosis of the right heart are observed in functioning carcinoid tumors.[14] It is known that serotonin produces capillary constriction in low concentrations but vasodilatation in higher concentrations. Studies relating to the possible role of tryptophane metabolism and the nicotinic acid-furfuryl reaction are planned.

Summary

A total of 183 patients with various diseases was tested with 5% nicotinic acid (niacin)-furfuryl ointment. Atypical reactions were noted in patients with active rheumatic disease and atopic dermatitis.

Patients with uncontrolled diabetes mellitus were found to be nonreactive or questionably reactive to nicotinic acid-furfuryl ointment, as compared with those with controlled diabetes.

Patients with mental disease react to nicotinic acid-furfuryl as do normal persons.

The nicotinic acid-furfuryl reaction was not altered experimentally by Coenzyme I or antihistamines. Internal administration of nicotinic acid slightly alters the reaction.

Steroids administered internally do not *directly* affect the reaction; locally applied they do not alter the cutaneous response.

The mechanisms involved in the nicotinic acid-furfuryl test remain unexplained.

17 E. Grace St. (19).

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ABSTRACT OF DISCUSSION

DR. WILLIAM B. GUY, Pittsburgh: The observations that Dr. Murrell derived from this study make interesting and understandable reading. It is an example of a very happy feature of our specialty that a clinician can participate in the investigative program in our field of medicine.

The author in this instance avoids what so many clinicians do when they venture into research. There is no attempt here to make statistics prove anything and no abstract conjecture in the fields of biochemistry or physiology. This is not meant to discredit these basic disciplines, but it is intended as a suggestion that we avail ourselves of the help of biostatisticians, physiologists, and chemists when we need them.

We have here another beam of light playing into the enigmatic dark of atopic eczema. Callaway previously reported finding an atypical response to nicotinic acid-furfuryl ointment in 18 out of 18 atopic eczema patients tested. Dr. Murrell apparently also found the reaction universally atypical in the atopics he tested.

Investigators who have previously studied this reaction in a variety of internal diseases have considered it a phase reaction, as Dr. Murrell stated, and by a phase reaction they mean such reactions as C-reactive protein and nonspecific hyaluronidase-inhibitor tests, tests which occur in acute inflammatory diseases with a general constitutional response and which revert to negativity when that constitutional response subsides.

They reported that these tests showed only atypical reactions in mildly inflammatory diseases, such as tuberculosis. This study reports the finding of an atypical response in several cases of uncontrolled diabetics and in two cases of scleroderma. This really stirs curiosity. As Dr. Murrell stated, as far as can be determined histamine or a histamine-like substance does not seem to be involved in this reaction. Alteration of nicotinic acid metabolism is somehow involved, as would be suspected from the fact that this material is, after all, an ester of nicotinic acid.

Although the mechanism of this altered reactivity excites interest, the possibility of its use as a diagnostic tool should not be overlooked. We all too often need help in diagnosing atopic eczema. Typical cases are easy enough, but in diagnosing hand eczemas and many nondescript eczematous processes we are frequently puzzled. A personal or familial history of atopy is often indefinite. Intradermal tests are equivocal, and eosinophil counts of the circulating blood and nasal smears are borderline. Yet, the eruption looks and behaves like atopic dermatitis. The "delayed blanch" reaction to acetylcholine injection has been an inconsistent finding in atopics in my experience. "White dermographism" has not been regularly found either.

If an atypical response to nicotinic acid-furfuryl ointment occurs in even a majority of atopics, it will help. I doubt that it will prove to be a universal finding when large numbers of patients are tested. I do not think that a consistent feature of this disease will ever be found, because I don't think one exists. If, in atopic eczema, it proves to be only a phase reaction accompanying acute episodes of the disease, it is not only a good diagnostic tool but, certainly, also a forward step in reasearch.

Reading this paper stimulated my interest to the degree that I ordered a supply of nicotinic acid-furfuryl ointment. It arrived in the middle of last week, and I immediately set to work testing myself, my office staff, and my associate. The reaction that we found, in what we assume are normal subjects, was very intriguing. There is an acute erythema with some edema, subjective sensations being nil at first. There is no itching, as there would be in an urticarial reaction. If anything, you could describe the sensation as one of hyperesthesia. You scratch it or stroke it with a sharp instrument, and you feel pain more than you do in other parts of the skin. Another interesting feature of the reaction is its long duration. On myself, the erythema remained for a period of three or four days. On the second or third day, the reaction was not itchy unless I scratched it, and then I could produce a dermographic effect on the patch of erythema. I almost had a reaction to show at this meeting, but it disappeared by early yesterday morning.

This presentation and its publication will undoubtedly stir up widespread interest in this material. Dr. Murrell's work is a noteworthy addition to our meager knowledge of atopic eczema. Any new information in any way related to this disease is welcomed by those of us who worry about our lack of progress in solving its mysteries.

DR. J. LAMAR CALLAWAY, Durham, N. C.: I am delighted that Dr. Murrell has attempted to investigate the elusive phenomenon which is demonstrated when nicotinic acid-furfuryl

ointment is applied to the skin. As I have stated before, our observations were purely clinical, and I have no satisfactory explanation for this reaction.

It is certainly intriguing that most, if not all, patients on whom I have made a daignosis of atopic dermatitis have shown the blanching atypical type of reaction. I think that the local application of nicotinic acid-furfuryl ointment is a useful adjunct in arriving at a diagnosis of atopic dermatitis, but it is certainly not an absolute diagnostic test.

DR. THOMAS W. MURRELL JR., Richmond, Va.: I want to thank Dr. Guy and Dr. Callaway for their discussion.

The most important thing experimentally about this work is the fact that up to the present time blanching has not been produced experimentally. The fact that we see this fairly uniformly in atopic patients is one of the most interesting phenomena with which we have had any experience.

Dermal Changes Following Abrasion

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With the Technical Assistance of Avis Gregersen, B.S., F.B.P.A., Los Angeles

The purpose of this paper is to report histologic and clinical observations at intervals up to four years, following both therapeutic and experimental abrasion of the skin.

Material and Methods

Thirteen patients from the Dermatology Service (Surgical Skin Planing Clinic) of the Los Angeles County General Hospital and from the private practice of one of us (S. A.) were utilized in this study. Some were relatively young, with acne scars of the face (the biopsy specimens included skin *not* acne scarred, however), while the majority were in the 70- to 80-year age bracket with multiple recurrent actinic keratoses of the face (farmers' or sailors' skin). In the case of two men whose backs were utilized for quantitative studies, the skin was normal senile skin.

The abrasions were performed with a motor-driven rotating abrasive instrument. A steel wire brush[28] was used on the earlier patients and a serrated steel disk or diamond-chip fraise (abrasive disk)[6] on the later ones. All were abraded with use of refrigerant anesthesia, a few of the early ones with ethyl chloride,[15] the remainder with dichlorotetrafluoroethane.[34] No differences were observed clinically or histologically that could be related to the type of abrading instrument or refrigerant used.

Forty-three biopsy specimens were obtained, and from these approximately 500 microscopic slides containing about 3,600 stained sections were examined. Serial sectioning was done when appropriate. The specimens were fixed in 10% formalin and sections were stained as follows: hematoxylin and eosin, Mallory stain (Milligan's modification), Van Gieson stain, Verhoeff's elastic fiber stain, Gregersen's modified silver nitrate stain for reticulum fibers, and Becker-Gregersen's silver nitrate stain for melanin pigment.

Dermal Changes Following Abrasion of Actinically Damaged Skin

It is obviously desirable to remove individual premalignant lesions from actinically damaged skin, whether by conventional techniques or by abrasion.[18,31] Theoretically, at least, it is equally desirable to remove the intervening potentially cancerous epidermis as well, because the cells of the epidermis which regenerate are derived from deep adnexal cells which have been less exposed to the damaging effect of sunlight.[2,5,6,9,22,23,35] It *may* follow then, that a relatively deep abrasion gives rise to a new epidermis with less susceptibility to cancer than does a very superficial abrasion.

We shall present clinical and histologic evidence to support the contention that abrasion has definite prophylactic value. However, it is not as effective as was anticipated, and its benefits decline with the passage of years. Furthermore, cosmetic problems are created by the very nature of epidermal pigment regeneration.

Biopsy specimens were taken from the border between abraded and nonabraded areas on the faces of patients with multiple

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From the Department of Dermatology, University of Southern California School of Medicine (Dr. Maximilian E. Obermayer, Chairman), and the Surgical Planing Clinic (Dr. Samuel Ayres III, Director), of the Dermatology Service, Los Angeles County General Hospital.

Miss Avis Gregersen, B.S., F.B.P.A., of the Department of Dermatology, University of Southern California School of Medicine, did the clinical photography, tissue stains, and photomicrography, assisted by Miss Beulah Malette, Mr. Herbert Harris, Miss Agnes Cherchian and Miss Rose Bly; the following resident physicians in dermatology at the Los Angeles County General Hospital gave technical assistance during the course of this study: Dr. Stuart Martel, Dr. Floyd Dornbush, Dr. Richard Mihan, Dr. Marian Brubaker, Dr. Roy Hiscock, and Dr. Charles Ellerding.

actinic keratoses and actinically damaged skin eight months to four years after abrasion. Clinically (Fig. 1), the *non*abraded skin shows hyperpigmentation and erythema in a retiform pattern and, in some areas, actinic keratoses. In contrast, the adjacent previously abraded skin is relatively *hypo*pigmented and has a homogeneous appearance. The pilosebaceous openings are intact; the hairs are normally pigmented, and there is no atrophy. The skin is firm and elastic and relatively free of fine wrinkles, compared to the adjacent flaccid nonabraded skin. Histologically, (Fig. 2) a melanin stain shows epidermal hyperpigmentation in the *non*abraded area, whereas, in the *post*abrasion portion of the specimen, it is markedly diminished. The epidermis in the *post*abrasion portion is comparable in thickness to the *non*abraded epidermis, but the rete ridges are less prominent (Fig. 3). In the *non*abraded portion, there is severe basophilic degeneration of the collagen in the upper cutis [15,24,30] in sharp contrast to the regenerated collagen, which stains normally. In addition, the collagen fibers in the regenerated area show a conspicuous horizontally striated pattern.

Thus, the new collagen is qualitatively different from the degenerated collagen it replaces and remains so for at *least* four years after abrasion. This is accompanied by a corresponding clinical change, as the regenerated skin has a more youthful appearance and greater degree of elasticity on palpation compared to the adjacent nonabraded skin. In this regenerated dermal tissue, elastic fibers are either entirely absent or very delicate, even up to four years after abrasion, but this is *not* clinically significant, since the elasticity of normal skin is now considered to be due chiefly to its *collagen* structure.[33] In fact, our results, which show the elastic fibers to be greatly diminished or absent in areas that clinically have a considerably *increased* elasticity, appear to confirm the correctness of this concept.

We have observed the occasional formation of new actinic keratoses, some advanced, with marked Bowenoid changes,

Fig. 1A.—Right side of the face of a 75-year-old man three years after abrasion for multiple actinic keratoses and actinically damaged skin. The area shows relative hypopigmentation and improved texture in contrast to retiform pigmentation and other actinic and senile changes on side of neck below jaw line, which was not abraded.

Fig. 1B.—Right side of the neck of 76-year-old fair-complexioned, blue-eyed man, showing nonabraded actinically damaged hyperpigmented and flaccid senile skin at left and upper right of photo. In contrast, the four-year postabrasion area in the center shows relative hypopigmentation. It is also relatively free of fine wrinkling and is more elastic on palpation. Islands of darker nonabraded skin at areas marked *X* are the result of failure to abrade the entire area evenly. On the right, indicated by an arrow, is a new actinic keratosis occurring within a previously abraded area.

Figs. 3A and 3B.—Figure 3A is a section from the nonabraded portion and 3B from the three-year postabrasion portion of the *same* biopsy specimen obtained from the border between abraded and nonabraded areas similar to that shown clinically in Figure 1. The epidermis is relatively flat in 3B, compared with 3A. Severe basophilic degeneration of the collagen in the upper cutis in 3A (extreme left of photo) is replaced by normally staining but horizontally striated collagen in 3B. The level of previous abrasion can be seen in 3B indicated by an arrow, below which coarse elastic fibers are present. None can be seen in regenerated dermal tissue above arrow. Elastic fiber stain; × 50.

Fig. 10.—Two weeks after abrasion of the face. The new epidermis is firmly attached. A zone of pale-staining newly regenerated dermal tissue is present above the level of recent abrasion, indicated by an arrow. The young fibroblasts show a horizontal arrangement. Elastic fibers are present only in the old dermis below the level of abrasion. Elastic fiber stain; × 50.

Fig. 11.—Two weeks after abrasion of the back. Delicate black argyrophilic fibers are present throughout the regenerated area blending with coarse collagen bundles (staining reddish-brown) at the level of recent abrasion, indicated by an arrow. Argyrophilic fibers are also concentrated at the dermoepidermal junction with small upward projections, as in normal skin. Marked irrgular acanthosis is present. Reticulum stain; × 50.

Fig. 14A.—Nonabraded area of the face of the same patient as in Figure 13. Elastic fiber stain; × 50 (for comparison with Fig. 14B).

Fig. 14B.—Ten months after a third abrasion of the face. Same patient as in Figure 14A. Rete ridges appear normally prominent compared with Figure 14A and vascular supply is similar. No elastic fibers can be seen in upper (regenerated) cutis, with resulting sharp line of demarcation at level of last abrasion indicated by an arrow. Below this, normal elastic fibers are present. Compare with elastic fibers in upper cutis in 14A. Elastic fiber stain; × 50.

Figure 1A

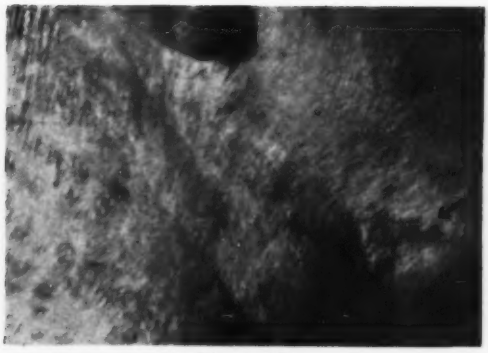

Figure 1B

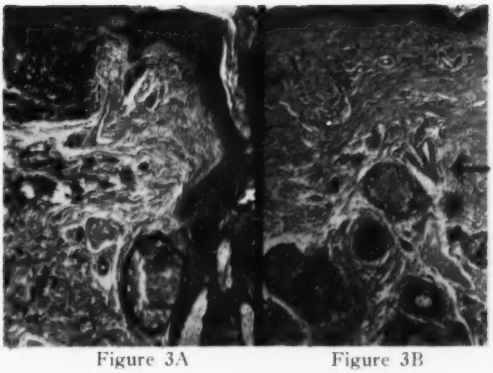

Figure 3A

Figure 3B

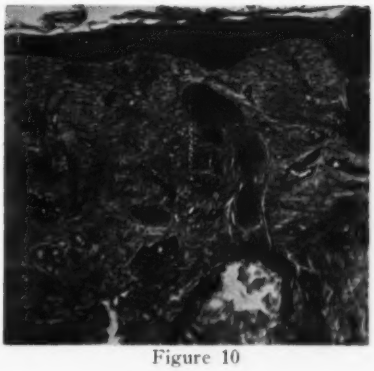

Figure 10

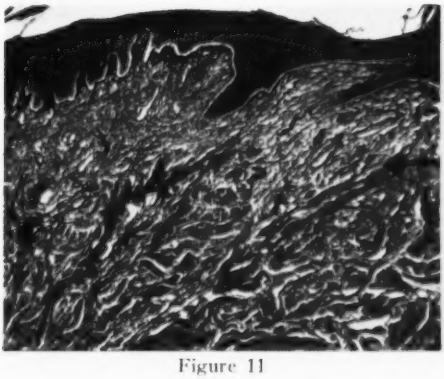

Figure 11

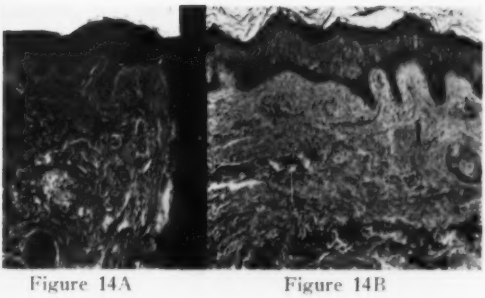

Figure 14A

Figure 14B

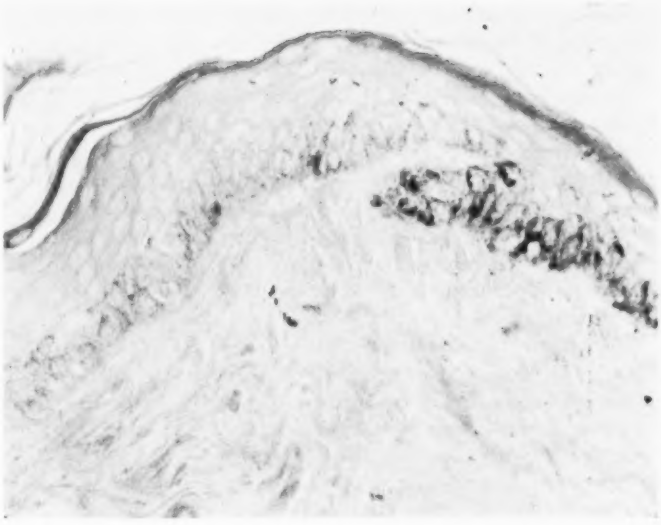

Fig. 2.—Biopsy specimen taken from border between abraded and nonbraded areas of patient, similar to those shown in Figure 1, eight months post abrasion. On the right is the nonabraded portion, showing marked epidermal pigmentation and prominent rete ridges, and on the left is the postabrasion portion, which shows considerably less pigment and is relatively flat. Melanin stain, reduced 15% from mag. × 400.

from as early as eight months to four years after abrasion (Fig. 4). It could be argued that the abrasion had been incomplete, leaving islands of epidermis which had premalignant changes already in progress. However, as Figure 4 illustrates, a zone of new collagen, 0.4 mm. or more in thickness, can be seen between the base of the keratosis and the old collagen below the level of abrasion. This clearly indicates that the abrasion had been sufficiently deep to remove not only the epidermis but most or all of the zone of basophilic degeneration as well and thus strongly suggests that these premalignant epidermal changes have arisen *de novo*. Furthermore, these findings are evidence *against* the concept held by some [12, 13,26] that basophilic degeneration of the collagen is an important cause of skin cancer and are in support of Montgomery's con-

Fig. 4.—New actinic keratosis occurring in eight-month postabrasion area. Note that there is a zone of new dermal tissue 0.4 mm. thick between base of keratosis and level of previous abrasion (arrow). This indicates that the old epidermis had been removed completely in this area by the abrasion.

tention that malignant epidermal changes developing in chronic radiodermatitis are not merely secondary to the dermal changes.[29]

Despite these observations, the abraded areas are considerably less prone to develop actinic keratoses than adjacent nonabraded areas, even in patients observed for four years after abrasion. Therefore, abrasion is *relatively* effective in the prophylaxis of premalignant lesions, though *not* as completely so as would be anticipated on theoretic grounds alone.

The failure of the previously abraded areas to approximate the color of the adjacent actinically damaged senile skin is undesirable from a cosmetic standpoint and indicates the necessity of abrading large areas, evenly and without leaving intervening gaps (Fig. 1). The procedure should be extended at least to the jaw line and should preferably include the neck in patients in whom cosmetic appearance is an important consideration. When the prevention of skin cancer is the chief objective, then this consideration is less important.

In contrast to fair-complexioned persons with actinically damaged skin, Negroes, or others racially pigmented, usually repigment to match the adjacent skin by about three months after abrasion, although subtle degrees of *hypo*pigmentation with or without *hyper*pigmentation may persist for a year or longer. In each of these situations, the newly regenerated epidermis tends to become pigmented to a degree that is genetically normal for that particular person. Thus, in the case of the person who is *racially* heavily pigmented, his "new" epidermis is essentially the same shade as the "old." On the other hand, the "new" epidermis of the fair-complexioned white person is pale, matching in essence the covered portions of his body or his face in infancy. It would not be expected to match the adjacent skin, pathologically altered by many years of sun exposure.

Quantitative Studies on Dermal Regeneration

In order to determine the amount of regeneration that occurs following abrasive therapy, experimental abrasion to a controlled depth was performed on the backs of two persons, intentionally creating long troughs with a sharp line of demarcation between abraded and nonabraded areas. Excision biopsies were performed at intervals up to three months after the abrasion. The trough, as seen in cross section, is obvious in biopsy specimens taken immediately after

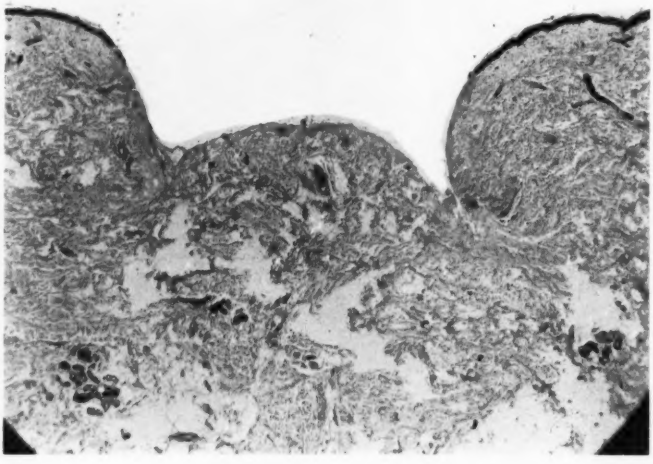

Fig. 5.—Cross section of intentionally created trough on back immediately after abrasion. Depth of trough averages 1.0 mm. and thickness of adjacent nonabraded skin measures 4.5 mm. exclusive of subcutaneous fat (total thickness not shown in photomicrograph). Reduced 15% from mag. × 20.

Fig. 6.—Section from edge of abraded trough shown in Figure 5 at 10 days post abrasion. Epidermal regeneration is complete, but new epidermis is unattached to dermis, and this space contains a cellular exudate. No appreciable dermal regeneration has occurred. The transient dedifferentiation of sebaceous glands following abrasion, described by Strauss and Kligman,[23] is also shown. Reduced 15% from mag. × 50.

Fig. 7A.—Low-power view of entire biopsy specimen, including trough in cross section, three weeks after abrasion. Compare with Figure 5. Crust still covers right half of trough. Floor of trough is 0.7 mm. below nonabraded surface. Full thickness of section is 4.5 mm. Reduced about 15% from mag. × 10.

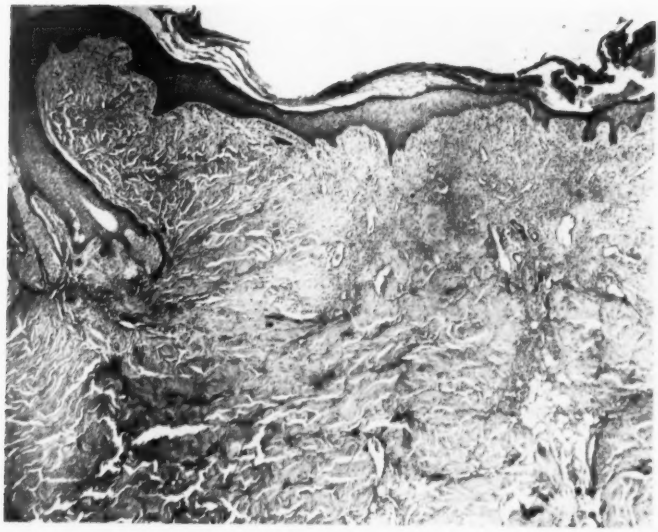

Fig. 7B. — Higher power of left border of trough, showing marked irregular acanthosis. Newly regenerated dermal tissue in center is in contrast to coarse collagen bundles of old dermis below and at left. Moderate lymphocytic infiltrate is present. Hematoxylin and eosin; reduced 15% from mag. × 20.

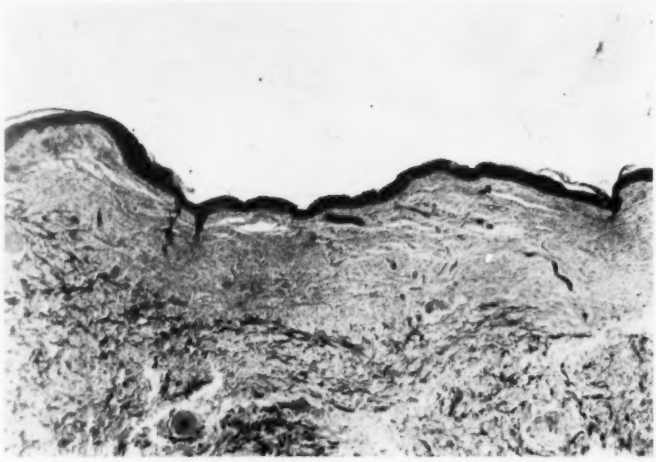

Fig. 8.—Three months post abrasion, from same area as previous three figures. Full thickness of section is not shown. One edge of the trough is seen at left. Epidermis is flat and devoid of rete ridges. Newly regenerated dermal tissue shows no elastic fibers at this magnification in contrast to nonabraded dermis. Of original 1.0 mm. depth of abrasion, approximately 0.5 mm. has regenerated, leaving a deficiency of 0.5 mm. The new skin is thus approximately 4.0/4.5 or 88% of its original thickness. Elastic fiber stain; reduced slightly from mag. × 20.

abrasion (Fig. 5). The depth of abrasion in a representative example measures 1.0 mm., whereas the total thickness of the adjacent nonabraded skin is 4.5 mm. At 10 days (Fig. 6), the groove is covered by epidermis but no *dermal* regeneration has occurred. At three weeks (Figs. 7A and 7B), the floor of the groove is 0.7 mm. below the level of the adjacent skin surface. Three months after abrasion (Fig. 8), 0.5 mm. has regenerated, still leaving a deficiency of 0.5 mm. clearly visible grossly before excision, as well as on the stained section. A similar experiment on the face gave comparable results.

Thus, after abrasion to the moderate depth of 1 mm., comparable to that attained in abrading acne pits of average depth,[23,32] dermal tissue regenerates substantially but not completely, so that the postabrasion skin is 85% to 90% of its original thickness. Most of this regeneration occurs during the second and third weeks after abrasion. The practical implication of these findings is that an appreciable, though not excessive, decrease in the total thickness of the skin occurs with regeneration following abrasive therapy and gives experimental support to the clinical observation that the results of inadvertent grooving or gouging by the abrading instrument or the creation of sharp lines of demarcation at the periphery of abraded areas tend to persist.

Even repeated abrasion results in only a moderate decrease in total thickness. For example, a stained section of skin taken 10 months after a third deep abrasion of the face measures 3.0 mm. in thickness, compared to 4.5 mm. for the preabrasion specimen obtained from a comparable area of the same patient.

These findings are consistent with Bishop's[4] observation that repeated thin excisions taken with a razor blade from the forearm did not result in appreciable thinning as long as the excision did not involve the reticular cutis but that deeper removal of tissue did result in visible thinning in the regenerated area.

Sequence of Events in Dermal Regeneration

We shall focus our attention primarily on the dermal component of regeneration as distinguished from the *epidermal* and *adnexal* components, since these have already received considerable attention.[2,3,6,7,11,16,17,20-23,32]

Three days after abrasion to a moderate depth, there is no evidence of *dermal* regeneration, whereas epidermal regeneration has definitely begun, with tongues of epidermal cells, derived chiefly from the adnexa, lying on the surface of the abraded dermis and in turn covered by the heavy

Fig. 9.—Three days after abrasion of the face. Tongues of epidermal cells (*EP*), derived from the adnexal cells remaining at and below the level of abrasion, have extended beneath the heavy crust (*C*) and are in direct contact with the surface of the abraded dermis (*D*), except in some areas, where a narrow zone of exudate has formed. No dermal regeneration has occurred. Reduced 15% from mag. × 50.

crust which has formed (Fig. 9). In some areas there is a narrow zone of amorphous material, staining pink with hematoxylin and eosin, between the new epidermal cells and the abraded surface. This is apparently an exudate, free of cells at this time, in the region where *dermal* regeneration later begins.

By *5 to 7 days* on the face and *10 days* on the back (Fig. 6), *epidermal* regeneration is complete but *dermal* regeneration is just beginning. Thus, *epidermal* regeneration clearly *precedes dermal* regeneration. The much richer supply of cutaneous adnexa on the face undoubtedly accounts for its more rapid epidermal regeneration. At this time, the new epidermis is very loosely attached to the underlying dermis or even unattached except at the periphery of the abraded area, the space between the new epidermis and the old dermis being filled with an exudate which now contains many round cells. This loose epidermal attachment is a good reason for not changing dressings frequently following abrasion, or better still, allowing a protective crust to form in lieu of a dressing.[14,17,23]

By *two weeks* after abrasion (Fig. 10), the new epidermis has become firmly attached. There is now a very conspicuous zone of *dermal* regeneration in the upper cutis, resulting in a sharp line of demarcation between the pale-staining newly regenerated dermal tissue containing numerous large young fibroblasts and new capillaries and the old deeper-staining collagen and elastic fibers below the level of abrasion. The new fibroblasts lie with their long axes almost uniformly in the horizontal plane, producing a conspicuously striated appearance. A reticulum stain (Fig. 11) shows a large number of delicate black argyrophilic fibers throughout the regenerated area, contrasting sharply with the coarse collagen bundles staining reddish-brown below the level of recent abrasion. The black-staining reticulum is concentrated at the dermoepidermal junction, with small upward projections, exactly as in normal skin. Since reticulum is generally considered to be immature collagen,[1,19,27,28] the presence of reticulum fibers, together with young fibroblasts in the uppermost cutis, is clear evidence of *dermal* regeneration. The transition of reticulum fibers into collagen at the level of recent abrasion gives additional support for this concept. Sometimes at two weeks and especially at *three weeks* (Figs. 7A, 7B, and 11), the epidermis, which contains no melanin, shows areas of marked irregular acanthosis, including about 3 mm. of the adjacent nonabraded epidermis.

By *two to three months* after abrasion (Fig. 8), the epidermis has lost its earlier hyperplastic feature and is now relatively flat and devoid of rete ridges.

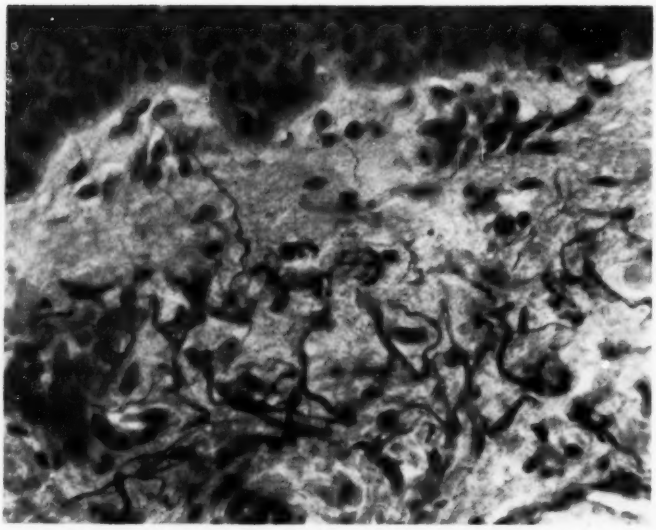

Fig. 12A. — Non-abraded portion of the same biopsy specimen as Figure 12B, to show the normal elastic fiber size and pattern in the upper cutis for comparison. This is normal senile skin of the back, unexposed to actinic damage. Compare also with Figure 3A. Elastic fiber stain; reduced 15% from mag. × 400.

Under low-power examination (Fig. 8), elastic fibers appear to be entirely absent in the regenerated area. In some specimens, however, with use of higher power (Figs. 12A and 12B), delicate new elastic fibers can be demonstrated, tending to run horizontally. In contrast, the adjacent non-abraded portion of the same specimen shows the normal, mainly vertical arrangement of elastic fibers in the upper cutis. When stained for reticulum, the regenerated dermal tissue now takes the reddish-brown stain of mature collagen.

Six months after abrasion of the face of a young white person, a pigment stain shows a normal amount of epidermal melanin. The blood vessels in the regenerated zone are considerably engorged. (Fig. 13). The cutaneous adnexa appear normal, though milia,[11] which are commonly seen between one and two months, can still be demonstrated. The epidermis is of normal thick-

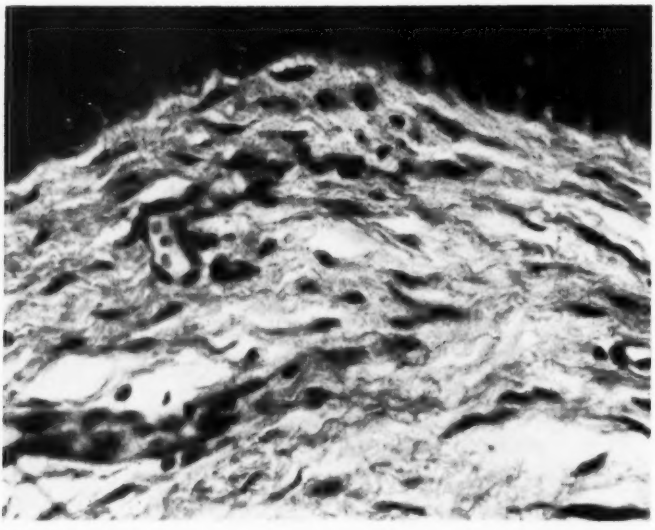

Fig. 12B. — Three months after abrasion of the back. Delicate elastic fibers are visible at this power, with a horizontal tendency, i. e., parallel to the epidermis and to the horizontally oriented new collagen fibers. Compare with Figure 12A. Elastic fiber stain, reduced 15% from mag. × 400.

Fig. 13A.—Nonabraded skin of the face of a 28-year-old man, same patient as shown in Figure 13B, for comparison. Hematoxylin and eosin; reduced 15% from mag. × 50.

ness, but rete ridges are substantially less prominent than in the preabrasion biopsy specimen obtained from a similar area on the face of the same patient.

Ten months after a third abrasion of the face (Figs. 14A and 14B), the rete ridges appear well developed when compared with a nonabraded control specimen and there is no longer increased vascularity. Elastic fibers are still virtually absent in the regenerated dermal tissue. This results in a sharp line of demarcation at the level of previous abrasion below which elastic fibers are normally prominent. By contrast, the nonabraded specimen from the same patient shows prominent elastic fibers in the upper cutis.

It is interesting to note that reticulum, which we have found to appear early in dermal regeneration, also appears early in

Fig. 13B.— Six months after abrasion of the face. The epidermis is comparable in thickness to that of a specimen from a similar area on the face of the same patient, though rete ridges are less prominent (compare with Figure 13A). Vascular engorgement and a postabrasion milium are seen. The adnexa appear otherwise normal. Hematoxylin and eosin; reduced 15% from mag. × 50.

fetal development—during the third month.[19] On the other hand, as we have seen, the regeneration of elastic fibers following abrasion is delayed and incomplete. This seems significant, since they do not appear in the fetal dermis until late—the sixth month—and also appear late phylogenetically.[25] Thus, wound healing recapitulates ontogeny, which recapitulates phylogeny.

Our observations on the early phases of epidermal and dermal regeneration are in essential agreement with the comprehensive studies of Gillman et al.[14] on wound healing in Thiersch-graft donor sites. Their material was not obtained from the face, as was a considerable portion of ours, but we have both found that epidermal regeneration precedes dermal regeneration, as long as the removal of tissue, whether by excision or abrasion, does not extend deep enough to destroy the cutaneous adnexa.

Summary and Conclusions

After abrasion to a moderate depth, the *dermis begins* to renegerate *after* the *epidermis* has *finished* regenerating. This occurs at about 1 week on the face and 10 days on the back.

Dermal regeneration is not quantitatively *complete*, but the postabrasion skin approximates 85% to 90% of its original thickness.

The newly regenerated dermal tissue at first stains as reticulum, but by two months after abrasion stains as mature collagen and has a horizontally striated pattern.

The postabrasion skin is relatively hypopigmented in fair-complexioned persons, in contrast to adjacent actinically damaged areas.

Abrasion has definite, though limited, value in the *prevention* of skin cancer and precancer.

The regenerated dermal tissue is deficient in elastic fibers—a histologic finding without clinical significance.

After abrasion, basophilically degenerated collagen in the upper cutis is replaced by normally staining collagen. A corresponding clinical change occurs, so that the regenerated skin is more elastic and youthful appearing than that of adjacent actinically damaged areas.

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ABSTRACT OF DISCUSSION

DR. STURE A. M. JOHNSON, Madison, Wis.: This excellent presentation by Dr. Ayres covers a step-by-step clinical and histological story of dermal changes seen following abrasion of the skin on different parts of the body, in different people, and age groups.

The authors emphasize the importance of the part that vitality, activity, and amount of adnexa play in the healing of the skin and in predicting the rate and type of regrowth that will take place. One would anticipate that regeneration of the epidermis and dermis would go hand in hand. Can the fact that they do not be explained?

I might suggest that nature, like the house-builder, wants the shingles on the roof before doing anything about the plastering. Although the authors make no comments regarding either clinical or histological observations on the effect of the duration of freezing before planing of the skin, I wonder whether Dr. Ayres might make some comment as to whether he has seen or feels that freezing causes any secondary effects on the underlying dermal structures which would make dermal healing slower than epidermal.

The incomplete effectiveness of abrasion of sun-damaged and premalignant skin in preventing recurrences of precancerous changes could be considered disappointing. On the other hand, one might emphasize as favorable the reduction in the number of recurrences and new actinic keratoses along with the rejuvenation process of wrinkled and flaccid skin. Many might prefer the homogeneous color and texture of the skin, freedom from fine and moderate wrinkles, and greater firmness and elasticity to the senile one that might be present. Could the hypopigmentation be prevented by guarded and regulated premature postoperative exposure to sunlight?

The opportunity to study restitution of dermal tissue following abrasive removal to a moderate depth is particularly interesting. The authors have shown that after the first abrasion, 85% to 90% of thickness returns, and after the second, 85% to 90% of that remain-

ing after the first, and so on. Fortunately, at this rate, there will aways be skin left even after repeated abrasions.

The demonstration by polarized light that the material seen in the foreign-body giant cells is most likely hair keratin must be pleasant news to many who have felt that they have been causing iatrogenic giant cells filled with pieces of steel brushes, disks, silica, and maybe even diamond chips from the tools of abrasion.

Dr. Francis A. Ellis, Baltimore: First, I wish to compliment Dr. Ayres on his beautiful paper. I have been interested in the regeneration of the skin following planing, and I should like to ask a few questions.

Does Dr. Ayres think that planing is good for cloasma? Since, in this session, we have had much discussion of pigmentation, it would be nice to know why cloasma may recur if you plane the entire affected area. Where does the re-formed pigment come from?

If 90% of the dermis regenerates in a few months, we can see why, for deep pits, planing is not the answer. Suppose we have pitted scars 4 mm. deep and we plane off 2 mm. of cutis, leaving a 2 mm. pit, then in several months, 90% of the planed dermis regenerates, we end with a pitted scar about 4 mm. in depth. We have practically not changed the depth of the pit at all. Well, you can say, surgically, you can remove that pit and replace it with a skin graft, but if you have a badly pitted face, that it is not very practical.

I was very interested in a slide that I saw from a case of xeroderma pigmentosa, in which one found a carcinoma arising from the bottom of a sebaceous gland, showing that in some cases at least the skin appendages do carry this cancer potentiality. Personally, I think that planing of the senile skin or precancerous type of skin is very practical. Here one replaces the epidermis and has under this a regenerated collagen. My experience is very limited and time will tell how soon the precancerous lesions recur in the regenerated skin. The final results will depend on many factors in the patient's planed skin.

Dr. Adolph Rostenberg Jr., Chicago: I should like to congratulate Dr. Ayres and his co-workers on an interesting clinical paper.

I rise primarily to suggest that techniques such as dermabrasion might be used to elucidate various problems. For example, an important point is, do lymphocytes invade the epidermis and become transformed into epidermal cells? This has far-reaching implications, particularly to those interested in immunology. The American anatomists, Andrews and Andrews, have asserted that they do, and Hagerman in Sweden has supportive evidence based on fluorescent-tagged lymphocytes. It occurred to me that this technique might be used to study such a point in the regenerating epidermis.

Dr. Ervin Epstein, Oakland, Calif: Our thanks and congratulations should go to Dr. Ayres and his co-workers for confirming, by careful microscopic studies, a fact based hitherto on clinical observation only. In other words, the actinically damaged senile skin regenerates normally after dermabrasion. Furthermore, it usually requires a great deal more new solar radiation before the precancerous senile changes recur. This is a big step forward in the prevention of cutaneous cancer in skin that has been chronically damaged to the point of the development of keratoses and epitheliomas.

We now have follow-ups of three to four years in patients with precancerous skin who have been planed. From the clinical standpoint, certain statements seem to be justified. The procedure decreases the future formation of keratoses and epitheliomas. This protection is not complete. Some recurrences develop shortly after planing. Furthermore, since the heredity of the epidermis is not changed by planing, continued exposure to radiation precipitates recurrences. However, if the person shows any judgment at all and takes his solar radiation in moderation, the patient who formerly could expect to look forward to spending the rest of his days as a "dermatologic cripple" can anticipate a life of comparative freedom from serious or frequent complications of this type.

Of course, the fact that the biopsy specimens showed no remaining epidermis after planing but recurrences developed anyway does not prove that all of the epidermis was removed unless serial sections were performed. However, speaking from the clinical standpoint, we have seen prompt recurrences in patients in whom the dermabrasion seemed to extend deeply into the corium. Therefore, we might assume that the recurrences develop in the new epidermis arising from the adnexa. According to this theory, the adnexal epidermis may have been damaged to a greater extent than we realize by the noxious radiations that affected the outermost covering of the skin. However, we cannot overlook the possibility that microscopic-sized islands of epidermal tissue may have survived the surgical procedure.

In my experience, there has been no difference in the postoperative pigmentary changes in these patients as compared to those planed for cosmetic reasons, provided the latter are sun-worshippers also. In my mind and in the minds of many others who have had extensive experience with this procedure in precancerous skin, the prophylaxis of malignant degeneration in the skin is the prime indication for planing today.

Dr. Hamilton Montgomery, Rochester, Minn.: I have no experience with the histopathologic changes following a planing operation. I wish, however, to call attention to a monograph by Dr. Shattuck Hartwell, of Muskegon, Mich., on the mechanisms and healing in human wounds, published by Charles C Thomas, Springfield, Ill., in 1955. Dr. Hartwell's monograph is based mainly on extensive study of surgical wounds when he was a Fellow at the Mayo Clinic. He showed that it was not the basal cells but the prickle cells that grew over the connective tissue in the cutis and if the dermal appendages were not involved then the cells from the dermal appendages would cover up the wound with a minimum of scar activity.

There are a good many articles from Durban, South Africa, by Gillman and his associates regarding healing of wounds under various conditions and reporting the fact that if the hair follicles are not destroyed one gets better results and less scarring. This fact applies as well to dermal abrasion.

Dr. Norman Epstein, San Francisco: I rise to point out a simple way of improving the skin as described here today, with precancerous, keratotic, actinic changes. To my mind, the first change is inflammatory and, often, these people have some seborrhea with it.

I have been able, and I know that many of you, too, perhaps, have been able to influence these skins by the simple use of hydrocortisone ointments before surgery is done. It is very much worth while to give them a trial, along with other measures of prevention, such as staying out of the sun and wind and so on. The liberal use of steroid ointments has been effective in some of my cases.

Dr. Marion B. Sulzberger, New York. I think that Dr. Ayres' paper shows how much one can discover by means of a simple approach to a clinical measure by studying it carefully, without complex and expensive equipment and with old and familiar techniques. I want to congratulate him.

I agree with Dr. Norman Epstein most emphatically that the combatting of the inflammatory component of these senile skins with their precancerous changes is an important therapeutic approach and a very beneficial one. In such cases I have also used hydrocortisone together with other agents, such as Vioform and the other hydroxyquinolines, to combat the inflammation and infection.

I should like to describe a simple experiment on one case that we carried out—that is, Dr. Alfred Kopf and Dr. Victor Witten and I—on a little girl with vitiligo. This was a case which did not respond to methoxsalen. This was one of the seven out of eight cases that does not respond. We abraded, by deep abrasion, a normally pigmented area of skin and also the vitiliginous skin and garnered the debris from each area separately and in as clean a fashion as we could. We transported the material gathered from the pigmented area to the abraded zone of the vitiliginous area and vice versa and attempted to let it heal in under sterile gauze dressings. Nothing happened. There was no pigment genesis with those cells that we carried over from the pigmented area to the vitiligo and probably no "take," either.

Dr. Samuel Ayres III: I particularly want to thank Dr. Johnson for his very generous comments in opening the discussion. He asked several specific questions. Regarding the relation of freezing and especially depth of freezing to the question of wound healing, I do not believe that that was an issue. There had been previous work done on wound healing, particularly by Gillman and his co-workers in South Africa on wound healing in Thiersch-graft donor sites, and our work in essence seemed to confirm theirs. Theirs did not involve the use of freezing, as our work did, yet the sequence of events in wound healing was similar. They stressed, and we also should like to stress, that in removal of tissue, whether by abrasion or by dermatome or whatever method, if the depth of the destruction is not such that the adnexa are completely destroyed, then the mechanism we have described is the correct one, in that the epidermis grows across first and then the dermal components regenerate, whereas, on the other hand, the older concept of wound healing is still true if one is speaking of a wound in which the total thickness of the skin, including the adnexa, is destroyed. Then, you have healing by so-called secondary intention, with true granulation tissue forming and subsequent epidermal bridging across from the wound margins. It is important, I think, to distinguish between those two mechanisms. However, I feel emphatically that the effect of freezing is not sufficient to

alter this mechanism, and I think that Strauss and Kligman pointed out, in their fairly recent article in the A. M. A. ARCHIVES of DERMATOLOGY, that the depth of freezing on the face, even on very prolonged freezing, is not greater than about 2 mm. The frozen skin seems to form a barrier to deeper freezing.

The question of sunlight exposure, deliberately and in a good amount, to prevent hypopigmentation, we have not tried as such, although these patients in general, in this senile, actinically damaged group, have been warned to avoid excessive exposure. However, we have in mind an experiment in which we will be able more objectively to try to deliver exposures of sunlight and artificial ultraviolet to controlled areas as compared to adjacent nonexposed areas, to see how much difference this makes.

I should like to emphasize that this is a relative hypopigmentation, not a complete absence of pigmentation, in these areas. In the younger age group with acne scars, for example, the pigmentation in the postabrasion areas generally assumes that amount that the person had at a somewhat younger age.

The question of the foreign-body giant-cell reaction seen at three weeks post abrasion was omitted in the final version of the presentation but was a very interesting phenomenon on which we hope to report in detail later.

In answer to Dr. Rostenberg, I have no answer on the lymphocytic infiltration of the epidermis. We are not looking for that specifically, so I do not recall that feature. But I should like to endorse his idea, certainly, that the general use of abrasion as a study tool is extremely useful and can be done in many different ways, particularly with relation to dermal structures which have not received too much attention as compared to epidermal and adnexal structures.

To Dr. Ellis, regarding the planing for chloasma, the fact that it does recur, with which I agree, in many cases, probably relates to the fact that there is some unknown factor that causes chloasma in the first place and, whatever it is, causes it to recur, just the same as the Negro skin tends to repigment to its normal degree. Certainly, planing is not the answer to a very deep pit. As we pointed out in a recent article (Feb., 1958) in *California Medicine*, if you fail to abrade to the full depth of the pit, then this dermal regeneration on all sides of the pit nearly reconstitutes the original architecture.

To Dr. Ervin Epstein, we did do serial sections on these, and I believe this was a bona fide occurrence; that is, a new occurrence of an actinic keratosis and not a failure to abrade away the epidermis adequately. I should certainly urge caution in treating radiodermatitis with abrasion. For limited areas, one can use it with caution, but, for large areas, such as the whole face, in which the adnexa have been destroyed, I should urge the greatest conservatism.

To Dr. Montgomery, I think the work referred to is that of Gillman and his co-workers, previously mentioned.

I have not had experience with the use of hydrocortisone ointment to combat the inflammatory aspect of actinic keratoses mentioned by Dr. Norman Epstein and by Dr. Sulzberger, but I think that it is most interesting.

Value of Patch Tests in Dermatology

Special Study of Follicular Reactions

S. WILLIAM BECKER, M.D., and MICHAEL PATRICK O'BRIEN, M.D., Long Beach, Calif.

The patch test has assumed its rightful place as a useful tool in the diagnosis of suspected allergic contact dermatitis (eczema). The original method of Jadassohn and Bloch has undergone modifications designed to insure continuous contact between the allergen and the epidermis (pressure method of Fernström) and use of transparent receptacles for contact with liquids and gases.[2]

Employment of patch-testing has varied greatly. In the late 20's and early 30's, routine patch-testing to a standard group of allergens was practiced by many institutions, but, at present, testing is usually to materials which may have been encountered in the patients' occupations or activities. Preemployment patch-testing and patch-testing to articles of clothing and various cosmetic or therapeutic preparations to be used on the skin are discussed by Schwartz et al.[3] Ayres[4] has suggested that pretreatment patch tests be made on patients who present possible occupational dermatitis with the various medicaments which might be used in therapy.

Purpose of Study

At the Long Beach Veterans Administration Hospital, a considerable number of patients have, in addition to primary dermatitis, secondary toxic (or allergic), more or less generalized dermatitis as a result of so-called autoeczematization, which has been reviewed recently by Young,[5] who studied 60 patients with "generalized autogenous eczema." Lipschultz[6] believes that the disorder constitutes allergic reaction to products of secondary infecting organisms, alone or in combination with substances derived from epidermal cells and keratin. Miescher[7] has shown that bacterial products, when used as patch tests, produce eczematous reaction. Most of our patients had positive bacterial cultures, almost exclusively coagulase-positive hemolytic Staphylococcus (Micrococcus) pyogenes var. aureus.

Anamnestic and clinical considerations have fallen short of establishing a satisfactory diagnosis of the primary dermatitis. It seemed, therefore, that patch-testing with a routine list of allergenic chemicals and the oleoresins of plants from this region might aid in identifying the original eruption as one caused by epidermal allergy, in case some reactions were positive, or possibly as one of functional nature, in case all patch tests were negative, as discussed by Becker and Obermayer.[8] It is, of course, always possible that the patient may be allergic to some substance or substances not included in the test materials.

The list of substances used is shown in Table 1. The tests were made with elastopatches, which were removed in 48 hours and the reaction recorded, with additional observation usually one or more days later. Results were recorded as negative or 1+, 2+, 3+, or 4+.

Results

The chemical allergens were applied to 110 patients, after the dermatitis had practically subsided, 69 of whom showed posi-

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From the Veterans Administration Hospital; Chief, Section of Dermatology (Dr. Becker); Senior Resident in Dermatology (Dr. O'Brien).

TABLE 1.—*Routine Patch Tests*

	Chemical
1.	Procaine hydrochloride (Novocain), 1%
2.	Tincture nitromersol (Metaphen), 1:200
3.	Merbromin (Mercurochrome), 2%
4.	Resorcinol, 1% aqueous
5.	Copper sulfate, 1% aqueous
6.	Formaldehyde, 2% aqueous
7.	Sudan III, 5% in olive oil
8.	Chromium trioxide (chromic acid), 1% aqueous
9.	Resorcinol, 1% alcoholic
10.	Mercuric chloride, 1:1,000 aqueous
11.	Nickel sulfate, 5% aqueous
12.	Ammonium fluoride, 5% aqueous
13.	Quinine hydrochloride, 1% aqueous
14.	Tetrabromofluorescein (eosin) powder
15.	Potassium iodide 25% in lanolin and petrolatum, in equal amounts
16.	Ammoniated mercury ointment, 5%
17.	Butamben (Butesin) picrate, 1% (nitromersol 1:5,000) ointment
18.	Whitfield's ointment and petrolatum, in equal amounts
19.	Ethylaminobenzoate (Benzocaine), 5% in hydrous woolfat (lanolin) and petrolatum, in equal amounts
20.	Crude coal tar ointment, 5%
21.	Ichthammol in petrolatum, 10%
22.	Iodochlorhydroxyquin, U. S. P. (Vioform) in petrolatum, 10%
23.	Sulfur in petrolatum, 10%
24.	Gum turpentine (50% in olive oil)

	Oleoresin
1.	Bermuda grass
2.	Chrysanthemum
3.	Cosmos
4.	Crab grass
5.	Downy brome grass
6.	False ragweed
7.	Geranium
8.	Johnson grass
9.	Lamb's quarters
10.	Poison ivy
11.	Poison oak
12.	Poison sumac
13.	Short ragweed
14.	Snapdragon

TABLE 2.—*Results of Chemical Patch Tests* *

	No.
Chromium trioxide (½% aqueous)	14 (12.7%)
Oto-Derm (mercuric nitrate)	13
Benzoic & salicylic acid (Whitfield's) ointment & petrolatum āā	12
Nickel sulfate (5% aqueous)	11 (10%)
Copper sulfate (1% aqueous)	8 (7.3%)
Ammonium fluoride (5% aqueous)	8 (7.3%)
Ammoniated mercury ointment, 5%	8
Ethyl aminobenzoate (Benzocaine) (5% in hydrous wool fat & petrolatum āā)	7
Crude coal tar ointment, 5%	6
Vioform (10% in petrolatum)	5
Procaine hydrochloride (Novocain), 1%	4
Butamben picrate, 1% / Nitromersol (Metaphen), 1:5,000	3
Gum turpentine (50% in olive oil)	3
Nitromersol tincture, 1:200	2
Merbromin (Mercurochrom), 2%	2
Resorcinol, 1% aqueous	2
Sudan III (5% in olive oil)	2
Mercuric chloride (1:1,000 aqueous)	2
Potassium iodide (25% in hydrous wool fat & petrolatum āā)	2
Resorcinol (1% in alcohol)	2

* Patients tested, 110; number reacting, 69. There were no reactions to the following chemicals: quinine hydrochloride (1% aqueous), tetrabromfluorescin (Eosin) powder, ichthammo (Ichthyol) (10% in petrolatum), and sulfur (10% in petrolatum)

tive reactions (Table 2). The reactions to nickel, chrome, copper, and fluoride were usually follicular or poral (recorded as folliculoporal) in nature. Oleoresins were applied to 56 patients, 16 of whom reacted (Table 3). The following patients presented significant reactions.

CASE 1.—A male Negro shoe-shiner, aged 45, was seen on Nov. 1, 1955, with severe dermatitis of all surfaces of both hands. He had had previous dermatitis of the hands in 1950. The eruption healed, and he was discharged on Dec. 12. He was seen with a severe recurrence on the same areas on May 29, 1956. The eruption receded under therapy, and patch tests to chemicals were applied. He reacted positively to chromium trioxide (chromic acid) with a folliculoporal reaction and to turpentine. Patch test to a brand of tan shoe polish was also positive.

In order to study the development of the reaction to chromium trioxide patch tests were applied and biopsy specimens were removed at hourly intervals up to 6 hours, then at 24, 36, and 48 hours (Fig. 1). At the end of one hour perivascular lymphocytic reaction was evident. This reaction slowly increased in severity until, in addition, at four hours (Fig. 2*A*) lymphocytic infiltrate was seen about the superficial portion of sweat ducts. At 24 hours, the reaction was identical but more pronounced (Fig. 2*B*). At 36 hours, the reaction was still more pronounced (Fig. 2*C*), while at 48 hours (Fig. 2*D*), perifollicular vesiculopustulation was evident. One specimen, taken 48 hours after removal of the patch test, showed pronounced dermal edema but no epidermal vesiculation (Fig. 2*E*).

Intradermal injection of 0.04 ml. of 1:100,000 solution of potassium bichromate, according to the method of Epstein, showed severe dermal edema with moderate perivascular lymphocytic infiltrate but no epidermal vesiculation (Fig. 2*F*).

Social study revealed that he was a definitely hostile, ingratiating person with a stammering speech defect so severe that he could scarcely speak.

CASE 2.—A plasterer, aged 65, who also worked with cement, was first seen on Dec. 10, 1957, with chronic dermatitis of 20 years' duration. The current eruption had been present for two weeks.

Fig. 1 (Case 1).—Folliculoporal patch-test reactions to 0.5% chromium trioxide. The lower patch had just been removed at 48 hours.

The dermatitis had started originally when a cast had been applied to the right hand after a fracture. Generalized vesicular eruption had followed. He had had periodic exacerbations after periods of work in dusty atmosphere. He had had an operation for gastrointestinal bleeding in 1955. He had arthritic deformity of the fingers, biceps tendinitis, and deltoid bursitis. He presented exudative dermatitis of the hands and feet. Patch tests were all negative, except a 2+ folliculoporal reaction to chromium trioxide. Intradermal injection of 0.05 ml. of 1:100,000 potassium bichromate revealed a clinically positive reaction after 48 hours. Microscopic section showed moderate perivascular lymphocytic infiltration, with dermal edema and slight intercellular epidermal edema. Diagnosis was made of probable exudative neurodermatitis. He developed an axillary abscess from which S. pyogenes var. aureus, coagulase-positive, was cultured.

TABLE 3.—*Results of Oleoresin Patch Tests*

Patch Test (56 Patients)	Reactions, No. (16 Patients)
Poison ivy	8
Poison oak	7
Poison sumac	6
Cosmos	4
Crab grass	2
False ragweed	2
Short ragweed	2
Chrysanthemum	1
Downy brome grass	1
Geranium	1
Johnson grass	1
Lamb's quarters	1
Bermuda grass	0
Snapdragon	0

CASE 3.—A single male electrician, aged 37, had had urticaria at the age of 4 months, dermatitis after infection at 9 months, and dermatitis at 4 years of age. He suffered a severe recurrence while in high school, in 1938. He had rheumatic fever in 1939, when the dermatitis became worse. He enlisted in the Air Force in 1939 and was discharged because of the dermatitis in 1943. Since that time he has worked primarily in the aircraft industry. His most recent work was as electrician, in which occupation he drilled through aluminum coated with zinc chromate primer. He is a food faddist and cooks his own food, and he may not have received an adequate diet.

He presented patches of dermatitis over many parts of the body (Figs. 3 and 4). Diagnosis was made of exudative neurodermatitis. After the dermatitis had improved, patch tests were performed to chemicals and oleoresins. The only positive reaction was to chromium trioxide. He was also positive to an aluminum disk coated with zinc chromate primer. Microscopic section revealed a folliculoporal reaction (Fig. 5) with perifollicular vesicopustules.

Scratch tests in the allergy clinic revealed 1+ reaction to beef and dried (brewer's) yeast. Intradermal tests revealed 1+ reactions to rye and almond; 2+ reactions to corn, buckwheat, peach, orange, celery, tomato, cashew nuts, peanuts, hazelnuts, English and black walnuts, all feathers, and kapok, and 3+ reactions to green peas, Brazil nuts, orris root, and house dust. Tests showed 2+ and 3+ reactions to hairs. Plant tests evoked 2+, 3+, and 4+ reactions to many plants.

Psychological evaluation revealed that he is a hyperkinetic person with a "machine gun" speech. He was considered to have chronic undifferentiated schizophrenic reaction.

In spite of therapy, his dermatitis appeared periodically in various areas and healed slowly and only partially.

CASE 4.—A farm helper, aged 64, was first seen on Sept. 27, 1955, with exudative dermatitis of five months' duration which had started on the right foot and spread to involve most of the trunk and extremities. He had done considerable spraying of

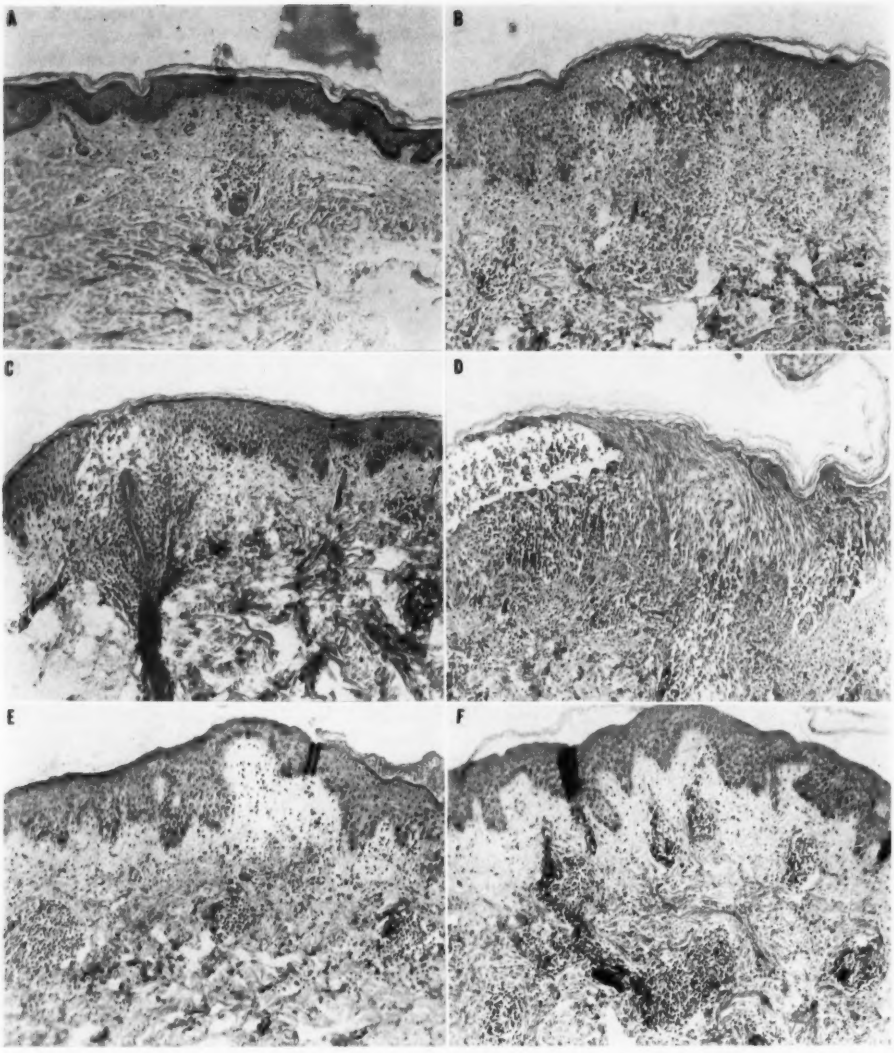

Fig. 2 (Case 1).—All magnifications reduced 25% from mag. × 100. *A*, 6-hour patch test reaction to 0.5% chromium trioxide. Perivascular and periductal lymphocytic infiltrate. *B*, (24 hours) dermal infiltrate and periductal epidermal spongiosis. *C*, (36 hours) periductal epidermal vesiculation. *D*, (48 hours) perifollicular vesicopustule. *E*, dermal edema two days after removal of patch test at 48 hours. *F*, 48 hours after injection of 0.05 ml. of 1:100,000 potassium bichromate solution.

trees with various chemicals. As the lesions healed, they became lichenified. Diagnosis was made of exudative dermatitis with lichenification.

General physical examination revealed no abnormalities, and ECG was within normal limits. Patch test showed 4+ folliculoporal reaction to nickel sulfate, 3+ folliculoporal reaction to ammonium fluoride, 2+ reactions to butamben (Butesyn) picrate and ethyl aminobenzoate (Benzocaine) and 1+ reaction to 5% crude-coal-tar ointment. He knew of no previous contact with these chemicals.

Serial patch tests to 5% nickel sulfate were biopsied at 8, 24, 36, and 48 hours. The findings are as follows: at 8 hours, mild perivascular lymphocytic infiltrate (Fig. 6*A*); at 24 hours, moderate

Figure 3

Figure 4

Fig. 3 (Case 3).—Dermatitis of hands.

Fig. 4 (Case 3).—Dermatitis of neck.

perivascular and periporal lymphocytic infiltrate and slight periporal epidermal edema (Fig. 6*B*); at 36 hours, the same, with slight aggravation (Fig. 6*C*); at 48 hours, the same, with increased epidermal edema (Fig. 6*D*).

The dermatitis was resistant to therapy and yielded only to steroids. When it was nearly healed, the patient suffered coronary occulsion and died.

CASE 5.—A Negro postal employee, aged 34, gave a history of having had dermatitis on the right foot and the popliteal regions for one year. He had hay fever and gave a history of allergic disease in his family. He presented exudative plaques of dermatitis on his right foot and in the popliteal regions. Under treatment, the exudative reaction disappeared and the plaques were lichenified (Fig. 7). It was concluded that the exudation had been caused by secondary infection and/or irritative therapy. Diagnosis was made of dry neurodermatitis. Biopsy specimens from the left popliteal space and the right foot showed epidermal hyperkeratosis, hypergranulosis, and acanthosis, with no intercellular edema or vesiculation. The dermis showed moderate perivascular lymphocytic infiltration. The picture was compatible with that of chronic dry neurodermatitis.

Patch tests to chemicals showed 1+ reaction (folliculoporal) to formalin and ammonium fluoride and 1+ reaction to 25% potassium iodide. Patch tests to oleoresins showed 2+ reaction to poison ivy, poison oak, and poison sumac (Fig. 8). Microscopic examination of the reaction to poison oak showed no change in the epidermis, with moderate perivascular lymphocytic infiltrate in the superficial dermis (Fig. 9). The reaction was interpreted as a sign of dermal allergy.

Scratch tests, carried out in the allergy clinic, showed 1+ reaction to egg white, rye, wheat, soy bean, rabbit meat, milk, and pyrethrum and 2+

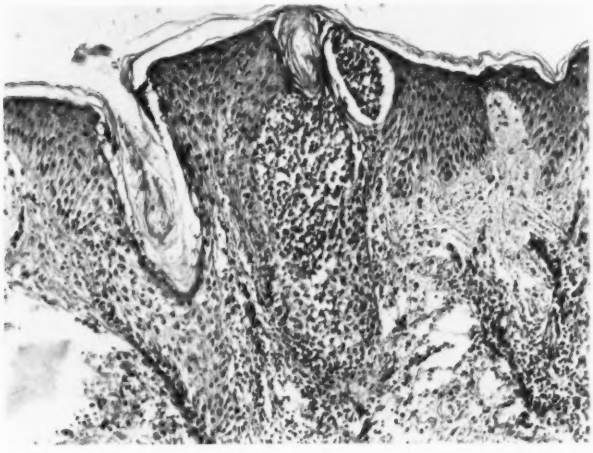

Fig. 5 (Case 3).—Follicular vesicopustule from 48-hour patch-test reaction to 0.5% chromium trioxide.

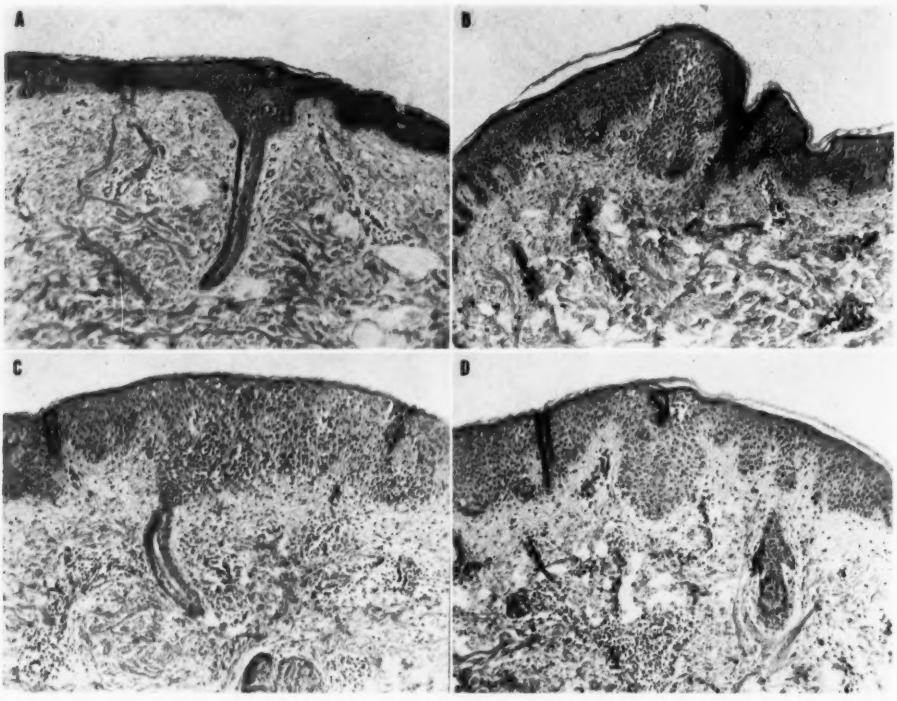

Fig. 6 (Case 4).—All magnifications reduced 25% from mag. × 100. Patch-test reactions to nickel sulfate. *A*, (6 hours) perivascular and periductal lymphocytic infiltrate. *B*, (24 hours) periductal epidermal edema. *C*, (36 hours) periductal epidermal edema. *D*, (48 hours) small periductal epidermal vesicle.

Fig. 7 (Case 5). — Lichenified neurodermatitis in popliteal region.

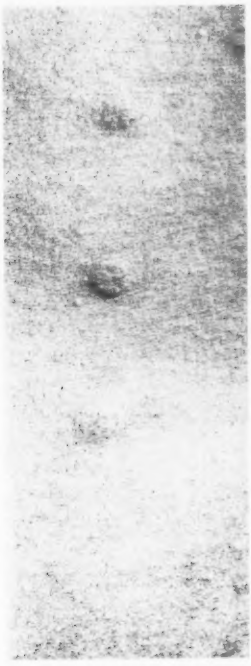

Fig. 8 (Case 5).—Positive 48-hour patch-test reactions to oleoresins of poison ivy, poison oak, and poison sumac.

reaction to ginger, goose and turkey feathers, and Endos dust.* There were positive reactions to plant proteins, including molds and fungi, varying from 1+ to 4+. Intradermal tests showed many 1+, 2+, 3+, and 4+ reactions to foods and environmentals. He was given a high-wheat diet under which the dermatitis continued to improve; hence, wheat was not considered causative or aggravative. He was given hyposensitizing injections to environmentals and late spring pollens. The eruption yielded slowly to treatment.

*Endos dust is a concentrated house dust marketed by the Endo Company.

Nature of Follicular Reactions

Papular or papulovesicular reactions to patch tests have been reported for many years and have been interpreted in various ways. Sulzberger[9] interpreted them as caused by primary irritation. Our finding of only 7.3% from copper sulfate and ammonium fluoride, 10% from nickel sulfate, and 12.7% from chromium trioxide would scarcely warrant such an opinion. We, therefore, believe that the reactions result from dermal allergy and not primary irritation. Epstein[10] intimated that folliculoporal reactions may either be allergic or follow primary irritation.

Schwartz et al.[3] gave the following definitions:

A primary cutaneous irritant is an agent which will cause dermatitis by direct action on the normal skin at the site of contact if it is permitted to act in sufficient intensity or quantity for a sufficient length of time . . . . A cutaneous sensitizer is an agent which does not necessarily cause demonstrable cutaneous changes on first contact, but may effect such changes in the skin that, after five to seven days or more, further contact on the same or other parts of the body will cause dermatitis.

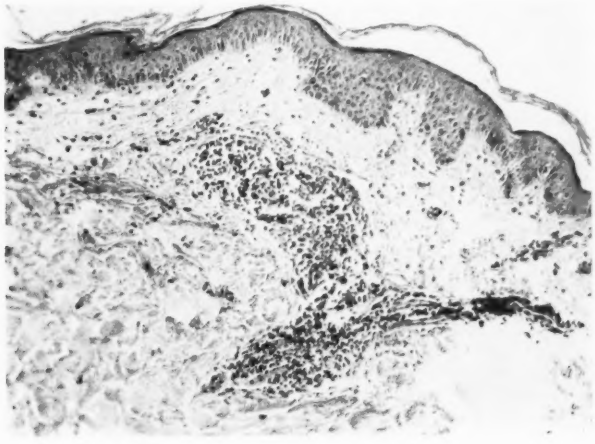

Fig. 9 (Case 5).—Forty-eight-hour patch-test reaction to poison oak. Dermal reaction only. × 100.

Combined Hypersensitivity to Certain Metals

In our small series, combined reactions were few in number. Eight patients reacted to chrome alone; five reacted to nickel alone, and two, to copper alone. One reacted to chrome plus nickel; two, to chrome plus copper; two, to nickel plus copper, and two, to all three. Epstein [11] reviewed the literature and expressed his belief that there is true cross sensitivity between nickel and copper but found none between nickel and chromates. Since chrome, nickel, and copper often elicit folliculoporal reactions, it might be advantageous to study the type of patients involved, i. e., those with dermal but not epidermal allergy (those who are prone to develop functional dermatitis but rarely, if ever, contact eczema). For instance, Simon's [12] microscopic illustrations of positive patch tests to human dander showed periporal reactions, which would seem to denote dermal rather than epidermal allergy.

Comment

The results of our patch tests were of considerable value in interpretation of the patient's primary dermatitis. The eczematous reactions, interpreted as representing epidermal allergy, signified that the patient's primary dermatitis may have been the result of epidermal allergic reaction, while positive folliculoporal tests suggested dermal allergy and that the primary dermatitis is more apt to have been functional in nature. If all tests are negative, primary functional dermatitis is also suggested.

Dermatitis from nickel and chromates is ably discussed by Epstein,[10] with an extensive review of the literature. Walsh [13] discussed chromate hazards in industry, and Hall [14] analyzed occupational dermatitis in the aircraft industry, where most eruptions were caused by chromates. Ekblad [15] placed shoe polish at the head of his list of eczematous sensitizers and stated that one particular brand was usually the offender. It is not known whether the tan polish contains chrome, to which our patient (Case 1) was allergic. Denton et al.[16] found sufficient chromate in cements in the United States to produce allergic reactions in hypersensitive patients, such as our Case 2.

Persistence of dermatitis after removal from all known contacts with chromates, as illustrated by our Case 3, conforms to the findings one of us (S. W. B.), presented in 1946 [17] and interpreted as functional dermatitis rather than eczema from epidermal allergy to chromates. Dermatitis in Case 3 started during infancy and recurred intermittently throughout life but was accentuated during his contact with chrome in the airplane industry. Strauss and Kligman [18] may have observed the same mechanism as in our Case 5 in their accentuation of dermatitis from 3-pentadecylcatechol by administration of substances to which the patients' dermis was allergic. They did not illustrate the microscopic picture of positive patch-test reactions, which could also have been dermal, as in our Case 5, with positive reaction to poison oak, and by Epstein,[10] in his Figure 5, a patch-test reaction with no evident epidermal vesiculation but with a pronounced dermal reaction.

Summary and Conclusions

Patch tests to chemicals and to oleoresins are carried out on 110 and 56 patients, respectively, after their partial recovery from extensive "autosensitization dermatitis."

Reactions obtained to chemicals in 69 patients were usually eczematoid or folliculoporal. Reactions to oleoresins in 16 patients were erythematous, edematous, and, at times, vesicular.

Serial biopsy in patients with folliculoporal reactions showed that the primary reaction is dermal, with secondary folliculoporal epidermal vesiculation, which was interpreted as fundamentally dermal in origin.

Folliculoporal reactions were found most frequently in patients with functional dermatitis. One nonfollicular reaction in a patient with neurodermatitis revealed, on

biopsy, pronounced dermal but no epidermal reaction to the oleoresins of poison oak.

Folliculoporal reactions to metals may result from the type of patient—dermally but not epidermally allergic—as seen predominantly with functional dermatitis.

Recurrent dermatitis after removal from industrial contact with chromates may be functional in nature.

Further biopsies on patients with apparently epidermal allergy may reveal that the site of reaction is in the dermis rather than in the epidermis.

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Primary Actinomycosis of the Upper Extremity

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This case of actinomycosis involving the hand and arm is noteworthy because of the unique location. Not only was the skin affected but also the subcutaneous tissue, muscle, periosteum, and axillary node of the right arm. No discernible history could be elicited of any injury, occupational contact, or endogenous foci.

Most cases of actinomycosis of the skin, reported in the literature, reveal a history of farm work or of trauma due to human bites or of fist blows to the mouth. The cases resulting from oral contact include three involving the hand; in each instance the patient had hit another person on the mouth (Cope,[1] McWilliams,[2] and Burrows[3]). Others in which oral contact was suspected were 14 cases of primary actinomycosis of the breast, reported by Davies,[4] and one, described by Robinson,[5] in which the infection was traced to a human bite.

Farm contacts were associated with 31 out of 67 cases of actinomycosis of the skin reviewed by Klaber.[6] Many of his remaining 36 histories were inconclusive. Other recorded cases include one of a horseback rider with an infected subgluteal bursa[7] and another of a trapper with extensive actinomycosis of the hand.[8] Two cases from farm areas of Italy were reported by Ronchese[9] and Finch.[10] No obvious traumatic injury was apparent in either of these cases. Milian[11] recorded a case of actinomycosis of the hand in which the original injury may have been caused by a rusty nail.

Report of a Case

Our patient, a 42-year-old Negro man, was admitted to the Dermatology Service at Roosevelt Hospital on April 24, 1956, with a swollen right arm and multiple draining sinuses. It is believed that the infection started, in 1953, with a small abscess on the medial aspect of the right hand. Other abscesses appeared on the arm but cleared after a short course of injections, presumably an antibiotic. The hand lesion remained static until January, 1956, at which time abscesses appeared on the arm and progressed to the axilla. The patient had received no treatment during 1954 and 1955.

His history revealed that during Army service in the South Pacific, in 1945, he had had a chronic dermatitis of the legs and an abscess in the left inguinal area which cleared after incision and drainage. In 1943, he had been adequately treated for syphilis. Since 1949, he had worked in the shipping department of a garment house, and no history of farm contacts or trauma from a human bite could be elicited.

The physical findings were essentially negative, except for the lesions on the right arm. The hand and forearm were covered with numerous abscesses and draining sinuses, some with vegetative granulation tissue. The hand and fingers were restricted in function, and the forearm was swollen to the elbow.

Laboratory Findings.—Hemoglobin, 13 gms.; WBC, 9,600, with 52% polymorphonuclear cells, 37% lymphocytes, 4% monocytes, 1% eosinophils. Urinalysis was normal. A roentgenogram of the right arm disclosed involvement of the periosteum of the radius and wrist bones, particularly the pisiform. The chest roentgenogram indicated no invasion of the disease there. Microscopic examination of slides made from the purulent axillary drainage revealed the typical "sulfur" granules. A biopsy specimen from the skin of one of the

The hand and forearm, showing the edema and draining sinuses.

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From the Dermatology Department of Roosevelt Hospital.

arm lesions showed the typical "ray fungus." Of the many types of cultures done, only the anaerobic blood culture grew colonies of Gram-positive, nonacid-fast diphtheroids, along with some pleomorphic Gram-negative organisms.

Diagnosis and Course of Treatment.—On the basis of the biopsy and culture, a diagnosis was made of actinomycosis.

After two weeks' therapy of 1,200,000 units of penicillin and 6 gm. of sulfisoxazole (Gantrisin) daily, the drainage stopped and the axillary lesions began to regress. The patient was discharged from the hospital May 15, 1956.

Treatment, consisting of 1,000,000 units of penicillin and 6 gm. of sulfisoxazole daily, was continued in the clinic until June 29, 1956. Thereafter, the penicillin was cut to 1,000,000 units three times a week until Sept. 4, 1956. At this time a new deep nodule developed on the patient's arm. He was admitted to the Bronx Veterans Hospital, where he received a total of 24,000,000 units of penicillin between Sept. 7, 1956, and Jan. 24, 1957, along with 6 gm. of sulfisoxazole daily. In May, 1957, when the patient was seen again in the Roosevelt Hospital Clinic, his right arm showed residual scarring but otherwise appeared almost normal in size. At that time he was receiving 600,000 units of penicillin three times weekly. On July 2, 1957, pathological examination of a newly developed lesion revealed the "ray fungus," but the organism did not grow on culture media. The patient received an additional 10,800,000 units of penicillin during the next two months. When last observed, in June, 1958, the man's arm appeared completely healed and there was no evidence of any new lesions developing.*

Comment

The number and extent of the lesions in this case was greater than in most of the instances reported. However, as in the other cases, the disease did not become systemic, even though the local lymph nodes became involved. Nocardiosis may closely resemble this type of skin actinomycosis and will often be systemic.

The presence of actinomycosis should be suspected in all chronic infections of the skin which do not respond to ordinary treatment. The diagnosis is made mycologically. The "sulfur" granules in the pus can at times be differentiated by the peripheral clubbing, but granules are also seen in nocardiosis, botryomycosis, and maduromycosis. In this instance, the biopsy specimen showed the "ray fungus," with peripheral clubbing, fine hyphae, basophilic staining, and consistently small spores.

In most of the reported cases, where an early diagnosis was made, it was based on pathological findings. The organism is difficult to grow, but a cultured organism is necessary for definite diagnosis because the Nocardia granule may simulate that of Actinomyces bovis. The fungus grows anaerobically at 37 C in four to seven days. When examined microscopically on a slide, Gram-positive nonacid-fast short fine-branching hyphae or diphtheroids are seen.[12] After studying more than 600 cases, Holm hypothesized that the disease was caused by a synergism between anaerobic microbes of the actinomycotic group and certain others, such as Actinobacillus actinomycetemcomitans.[13] This then could account for the Gram-negative coccobacillus we observed in the case reported here.

There is some disagreement in the literature as to whether the etiological agent in man should be called A. israeli or A. bovis, but the latter is the generally preferred designation.

Penicillin is now the most effective drug for actinomycosis and should be used in high doses over a long period of time. Supportive measures, such as bed rest and blood transfusions, are helpful. In the past, single lesions of the skin were frequently removed by surgery. Cope believed that a vaccine and iodides as well as surgery promised the best results.[1] Milian's patient, whose condition resembled ours, was treated with intravenous lipoidal and Lugol's solution and ultraviolet and roentgen therapy.[11] Burrows prescribed 4,800 grains of potassium iodide over a period of 51 days. His patient had not previously responded to sulfanilamide.[3] In 1953, isoniazid was used successfully in a case involving the cervicofacial area.[14]

* This case was presented at a meeting of the New York Academy of Medicine, Dermatology Section, on May 1, 1956.

Summary

A case of primary actinomycosis extensively involving the right hand and forearm is presented.

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Keratosis Blennorrhagica (Reiter's Disease?) and Its Treatment

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The keratotic skin lesions of keratosis blennorrhagica, which usually follow gonorrheal urethritis and polyarthritis, have been treated with many drugs, but none has found universal approval. In recent years the antibiotics and the corticosteroid hormones have been used with varying success, ranging from complete cure to little or no effect whatsoever.

It is difficult to evaluate the true benefit of therapeutic agents in keratosis blennorrhagica because (1) the condition is usually self-limited and (2) the disorder is encountered too infrequently for any investigator to have an adequate number of control cases.

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Division of Dermatology, University of Miami School of Medicine (Dr. Albert) and Chief of Medical Service, U. S. Army Hospital, Landstuhl, Germany (Dr. Crone).

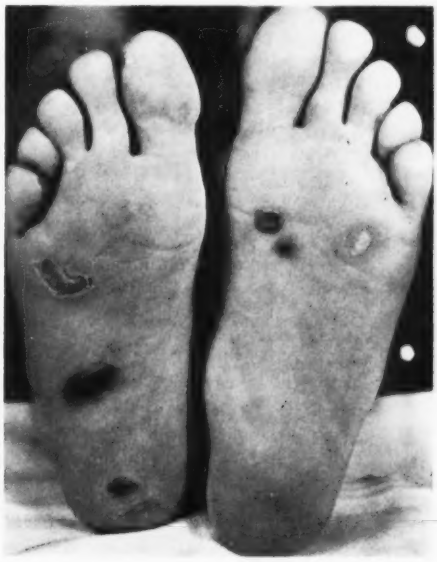
Fig. 1 (Case 1).—Lesions of penis: balanitis circinata.

The purpose of this paper is to review some of the literature on the treatment of keratosis blennorrhagica and to report our experience with the use of the antibiotics and corticosteroid hormones.

Report of Cases

CASE 1.—A 33-year-old white soldier developed gonorrheal urethritis and was treated with 1,800,000 units of procaine penicillin. One week later he developed arthritis of the right fifth toe, the right fourth finger, the right knee, and the left ankle. The urethral discharge cleared uneventfully after the penicillin treatment, but one month later he developed skin lesions on the glans penis (Fig. 1); on the soles of both feet (Fig. 2); on the interdigital areas between the third, fourth, and fifth toes of both feet, and in the web between the third and fourth fingers of the left hand. (See Case 2 for description of skin lesions.) He was admitted

Fig. 2 (Case 1).—Early lesions of sole contain a cheesy material and have a thickened covering.



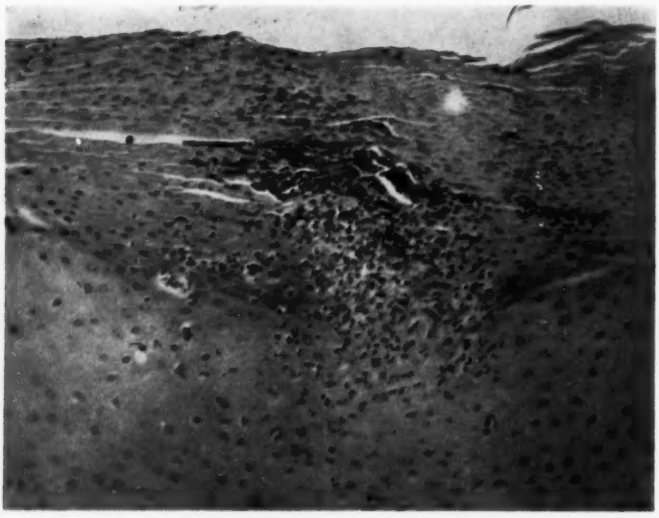


Fig. 3 (Case 1). — High-power magnification of upper epidermis of sole, revealing hyperkeratosis, parakeratosis, and intraepidermal aggregates of polymorphonuclear leukocytes.

to an Army Hospital in Germany for diagnosis and treatment.

Laboratory data revealed a white blood cell count of 11,000 per cubic millimeter, with a normal differential count; the hematocrit was 39%; the sedimentation rate, 44 mm. in one hour (Wintrobe); serologic test for syphilis was negative. Urinalysis was normal. Gram stains and cultures of the skin lesions were negative. A biopsy specimen of one of the skin lesions on the sole revealed the typical changes seen in keratosis blennorrhagica (Fig. 3). Gram stain of the tissue section failed to reveal gonococci.

The patient was treated with a combination of 1,200,000 units of procaine penicillin and 1.0 gm. of streptomycin intramuscularly daily for 10 consecutive days. He was also given 5 gm. of acetylsalicylic acid daily. The skin lesions began to improve after the fifth day of treatment, but they did not clear completely until five days after the penicillin and streptomycin were stopped. Only minimal improvement was noted in the arthritis. Treatment was continued with 5 gm. of acetylsalicylic acid daily as well as physical therapy. He gradually improved, and three months later he was free of joint symptoms and on full activity.

Case 2.—A 20-year-old white Marine developed gonorrheal urethritis three days after sexual exposure and was treated with 1,800,000 units of penicillin. The urethral discharge persisted, but gonococci could no longer be demonstrated. Two weeks later he developed a sterile bilateral conjunctivitis. Two weeks after this he developed arthritis of both knees, elbows, shoulders, left ankle, and left thumb. Aspiration of the left knee revealed no bacteria on smear or culture. Two weeks after he developed arthritis he noted skin lesions of both feet and the glans penis. At that time he also developed lesions in his mouth. Treatment with acetylsalicylic acid, sulfisoxazole (Gantrisin), oxytetracycline, streptomycin, and phenylazodiamino-pyridine hydrochloride (Pyridium) failed to cause improvement. On admission to an army hospital in Germany his temperature was 101 F (oral). Friable ulcerated lesions covered with a grayish membrane and surrounded by an erythematous halo were present on the gums,

Fig. 4 (Case 2).—Early lesions of the sole. No gonococci are present in the skin lesions.

Fig. 5 (Case 2).—The lesions shown in Figure 4, three weeks later. Some pustules have opened, revealing an erythematous base.

Fig. 6 (Case 2).—The lesions shown in Figures 4 and 5, one month later, reveal further extension.

the buccal mucosae, and the palate. Discrete vesicular skin lesions, ranging from 3 mm. to 1.5 cm., were present on both soles, the lower part of the right leg, and the glans penis. The skin lesions suggested an iris design at first, with brownish centers surrounded by a yellowish margin which was in turn bordered by an erythematous area. When these vesicular lesions were opened, a cheesy content was revealed. Dirty-brown, heaped-up crusts later formed on the remaining erythematous base. The lesions later coalesced to cover the entire plantar surface of the foot (Figs. 4, 5, and 6). As the disease progressed, new lesions appeared over the entire body. In the axillae, groins, and buttocks there developed confluent plaques. The nails of both hands and feet became thickened and discolored and were elevated from the nail bed by a heaping up of underlying keratotic material (Fig. 7). Urethritis was not present. Acute arthritis (swelling, heat, and redness) was present in both knees, elbows, and shoulders and the left ankle and left thumb. Conjunctivitis was present in both eyes.

Fig. 7 (Case 2).—Changes in the hand one month after the onset of skin lesions. The nails are elevated by underlying keratotic material.

Laboratory data revealed a white blood cell count of 11,500 per cubic millimeter, with 87% neutrophils, 12% lymphocytes, and 1% eosinophils; the hematocrit was 45%; the sedimentation rate was 31 mm. in one hour (Wintrobe); urinalysis was normal. The biopsy specimen of one of the skin lesions revealed that the epidermis was edematous, with thickened rete ridges, marked parakeratosis, and hyperkeratosis and several intraepidermal aggregates of polymorphonuclear leukocytes. A Gram stain of the tissue section revealed no bacteria. The changes were consistent with keratosis blennorrhagica. Serum protein electrophoresis revealed a total protein of 6.3 gm. %; albumin, 2.72 gm. % (43.2%); α_1-globulin, 0.86 gm. % (13.6%); α_2-globulin, 1.05 gm. % (16.7%); β-globulin, 0.82 gm. % (13.0%); γ-globulin, 0.85 gm. % (13.4%).

The patient was treated with a combination of 60 units of intramuscular corticotropin (ACTH), 1,200,000 units of procaine penicillin, and 1.0 gm. of streptomycin intramuscularly daily. There was some improvement in the arthritis, but new skin lesions continued to appear, and despite this therapy the patient's condition became progressively worse. The penicillin and streptomycin were stopped after two weeks, and the corticotropin was gradually reduced and stopped after three weeks of therapy. In the next 30 days various drugs were administered without benefit, including acetylsalicylic acid, tetracycline, erythromycin, and vitamin A. After more than three months of illness, the patient had lost 60 lb. and could hardly move about in bed because of his arthritis. His hematocrit reading had fallen to 36%, and his sedimentation rate had increased to 50 mm. in one hour. At this point, 50 mg. of prednisolone was administered daily in divided doses. After 24 hours of treatment the patient became afebrile, his arthritis showed remarkable improvement, and his appetite increased. After three days of prednisolone treatment, the patient, who had previously been bedridden for three and one-half months, was able to walk with help. There was only a slight improvement in the old skin lesions, but fewer new lesions appeared. The prednisolone dosage was kept at 50 mg. daily for a week and was gradually lowered by 2.5 mg. every 2 or 3 days for a total course of 50 days. During this time he had regained 40 of the 60 lb. he had lost during his illness and his skin had cleared completely. His hematocrit had risen to 49%, and the sedimentation rate had fallen to 8 mm. in one hour. His joints were normal. A follow-up report seven months later revealed that the patient was completely well and that there was no residual joint damage.

Comment

Etiological Considerations.—Although most of the reported cases of this condition are associated with gonorrhea, Ladany and Hughes,[1] in 1946, were able to find 34 cases of keratosis blennorrhagica without associated evidence of gonorrhea. This included 13 cases interpreted as Reiter's syndrome. Although this syndrome consists of a symptom triad of urethritis, arthritis, and conjunctivitis, gonococci have never been demonstrated and skin lesions were not included in Reiter's original report. Balanitis circinata was subsequently reported in some cases of Reiter's syndrome, and Wiedmann first reported from Austria that skin lesions identical to those of keratosis blennorrhagica were present in Reiter's syndrome. Later, Lever and Crawford[2] introduced to the United States the concept that Reiter's syndrome and keratosis blennorrhagica may be identical. Since Lever and Crawford's[2] report several American and English authors[3-7] have reported that the lesions of keratosis blennorrhagica may be present in Reiter's syndrome. Hall and Finegold[6] reported mucocutaneous lesions in all 23 of their cases of Reiter's syndrome, 5 of whom developed the generalized lesions of keratosis blennorrhagica. Since 1946 there have also been three reports of Reiter's syndrome with keratosis blennorrhagica, from Scandinavia. As a result of these publications there is increasing doubt of the gonorrheal etiology of keratosis blennorrhagica. Although there is a striking similarity between keratosis blennorrhagica and Reiter's syndrome, their precise relationship must await the unequivocal demonstrations of their etiology.

Treatment.—Despite the fact that most patients with keratosis blennorrhagica tend to recover spontaneously after several months, there is still a great need for effective treatment. A few deaths have been reported from this condition, and occasionally ankylosis of the joints has occurred.

Various therapeutic agents, such as autogenous vaccine, 1% solution of merbromin intravenously, massive doses of vitamin A, and fever therapy, have all had their vogue but have largely been abandoned as valueless.

The sulfonamides and various antibiotics have been used more recently. Spencer [8] claimed cure of a case of keratosis blennorrhagica with sulfathiazole, whereas Carr and Friedman [9] emphasized the uselessness of the sulfonamides. Emmet [10] and Miale and Singletary [11] reported success with the use of penicillin, but others [1,4] have found penicillin valueless. Cameron [7] reported cure of one case with chlortetracycline, but he observed no effect from it when used in another patient. Chinn and colleagues [12] as well as Thompson and colleagues [13] reported successful treatment of their cases with streptomycin. However, Myerson and Katzenstein [15] as well as Ikejiani [16] found streptomycin valueless. Shallard and Kanee [14] found no benefit from penicillin and streptomycin when used alone but noted dramatic success when these drugs were combined with 20 units of corticotropin, given intravenously over a 10-day period.

Myerson and Katzenstein [15] were the first to report successful treatment of keratosis blennorrhagica with intramuscular corticotropin. Two women, who were sisters-in-law, were successfully treated with corticotropin by Ikejiani.[16] Penicillin, streptomycin, chlortetracycline, vitamin A, and typhoid vaccine were found to be valueless in his patients. Hall and Finegold [6] found corticotropin did not benefit three cases of Reiter's syndrome with cutaneous lesions.

Cortisone was found ineffective in the treatment of keratosis blennorrhagica by Beck [18] and by Myerson and Katzenstein,[15] but Schwarz and Kingma [17] reported a prompt cure when cortisone was used in conjunction with penicillin.

Our first patient showed a clearing of his skin lesions after 10 days' administration of penicillin, streptomycin, and acetylsalicylic acid. Only minimal improvement was noted in the arthritis. The arthritis eventually improved on symptomatic doses of acetylsalicylic acid and physical therapy.

That the improvement in the skin lesions may have been fortuitous is suggested by the fact that our second patient did not improve on penicillin and streptomycin and that he actually developed new lesions while taking these drugs. In this second patient, corticotropin caused temporary improvement in the arthritis but the skin lesions were unaffected. Various other drugs, including tetracycline, erythromycin, and large doses of vitamin A, had no effect on the disease. There can be no doubt of the striking improvement in the patient's general condition within 24 hours after administration of 50 mg. of prednisolone daily in divided doses. A progressive downhill course was abruptly changed to one of steady improvement, manifested by a 40 lb. weight gain and complete clearing of his arthritis and skin lesions. Prednisolone apparently effected complete cure of the patient, whereas corticotropin only caused temporary improvement in his arthritis.

It is our impression that antibiotics do not alter the natural course of the disease but are of value in treating any secondary infection accompanying the condition. The corticosteroid hormones aid recovery by improving the arthritis and general well-being of the patient and are thus of value when given in the proper dosage.

The lack of consistent response to antibiotics is against the specific gonorrheal cause of this condition, whereas the response to corticosteroids is in favor of a possible allergic etiology.

Summary

The treatment of keratosis blennorrhagica is reviewed, and the difficulties in evaluating the true benefit of therapeutic agents in this disease are discussed.

Two patients with keratosis blennorrhagica are reported and the management of their illnesses discussed. There was prompt clearing of the first patient's skin lesions when a 10-day course of penicillin and streptomycin was given during the second month of his illness, but there was little effect on the arthritis. The second patient showed a complete and striking response to prednisolone after other therapy, including corticotropin (ACTH) and various antibiotics, had failed. It is suggested that pred-

nisolone be used in future cases of keratosis blennorrhagica in order to further evaluate its effectiveness.

No conclusion can be made as to the etiology of keratosis blennorrhagica at present, but its striking similarity to Reiter's syndrome is discussed. It is noted that skin lesions identical to those of keratosis blennorrhagica are being found in increasing numbers of cases of Reiter's syndrome.

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Erythroplasia of Queyrat

Report of a Case with Recurrence After Cessation of Topical Hydrocortisone

WILLIAM B. REED, M.D., Burbank, Calif.

A persistent penile plaque without skin involvement elsewhere on the body presents a puzzling problem. One must rule out erythroplasia of Queyrat by biopsy, since benign lesions may clinically give the same appearance. Blau and Hyman[1] point out that three diagnoses can be made histopathologically. They are Bowen's disease of mucous membrane (erythroplasia of Queyrat), benign inflammatory dermatoses of the mucous membrane, or plasmacytoma penis.

Fournier and Darier,[2] in their original description of erythroplasia, separated the disease into a benign and malignant type, depending on the presence or absence of malignant dyskeratoses. Nevertheless, the term erythroplasia has become synonymous with precancerous lesion requiring radical removal. Sachs and Sachs,[3,4] although retaining the term, have successfully treated lesions with neoarsphenamine topically, thus denoting the benign character of the lesions. Sulzberger,[5] in his excellent article on persistent penile plaques, gives the history of the first reported case[6] of erythroplasia in the United States, who had a persistent penile plaque since 1933 without malignant degeneration. With hydrocortisone acetate, 1%, and wet dressings (1954), there was complete clearance in 18 days. However, whether recurrence developed after therapy was unknown. Herein is a report of a case with recurrence of erythroplasia after such therapy.

Submitted for publication Oct. 29, 1958.

Instructor in Dermatology, University of Southern California School of Medicine, Los Angeles.

Report of Case

A 49-year-old telephone executive, uncircumcised, developed in August, 1957, a slowly growing asymptomatic plaque on the glans penis. However, because of the persistence of the lesion, the patient came for treatment in December, 1957. The plaque, well defined in its borders, measured about 2 in. in diameter, with some involvement of the coronal sulcus. The surface was nonexudative and almost velvety in texture, while the color was a brilliant violaceous red. Biopsy was performed at this time. Patient was given 1% hydrocortisone acetate cream with neomycin, with complete clearance in one week. With the discontinuance of medication for one month, the lesion appeared again in the same location and with the same

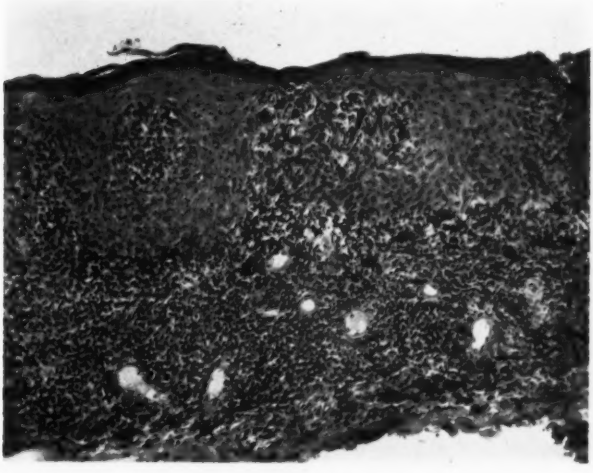

Fig. 1. — Low-power view, showing the acanthotic epithelium and the intense inflammatory reaction in the superficial dermis; × 130.

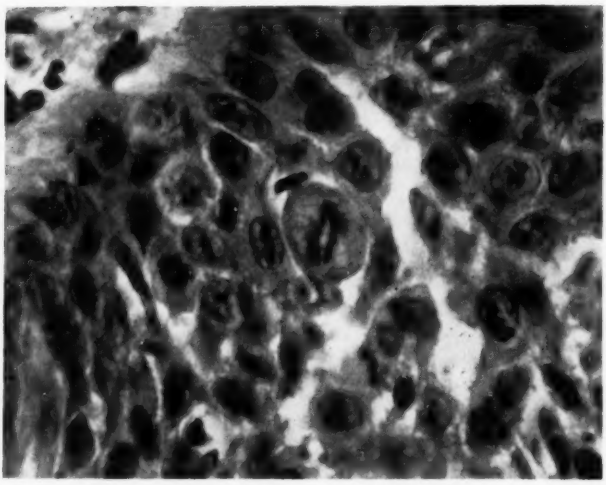

Fig. 2.—Two mitotic figures, found in the acanthotic epithelium; ×850.

clinical appearance. The patient was placed on 1% hydrocortisone acetate for two months, with again complete disappearance of the lesion. However when seen in July, after no medication for nearly three months, he showed a slight recurrence. The patient has so far refused circumcision.

He has had no other dermatoses which one would expect to localize on the glans penis: i. e., psoriasis, lichen planus, distinctive exudative discoid and lichenoid chronic dermatoses, and lichen nitidus. He takes no medication that could give a fixed drug eruption. Physical examination revealed no inguinal lymphadenopathy.

Pathological Examination

The epidermis is somewhat acanthotic, with rete processes that are peg-shaped. There are occasional mitotic figures, but not of abnormal configuration. The surface is covered with a parakeratotic epithelium. In the superficial dermis, there is a tremendous reaction of small round cells, wandering connective tissue cells, and numerous plasma cells.

Diagnosis.—Benign erythroplasia or balanoposthitis chronica circumscripta plasmacellularis. (Slides were read by Drs. Wilbert Sachs, Perry Sachs, and H. Montgomery.)

Comment

This patient represents a penile plaque that recurs after therapy without histopathologic signs of malignancy. However, because of the constant irritation from being uncircumcised, there is danger of malignant degeneration starting in an area of chronic inflammation on a mucous membrane. Blau and Hyman,[1] in their series of 62 American cases reported as erythroplasia, show that only 16 had histologic evidence of malignancy. Thirteen of these malignant cases were in the uncercumcised.

The term erythroplasia is no longer a good designation for this benign condition, for it connotes a precancerous lesion. The term plasmacytoma penis is clumsy, for it connotes a tumor of plasma cells, which are only a part of the inflammatory cells of this chronic lesion. Balanoposthitis chronica circumscripta plasmacellularis is an accurate description of the condition, but it is certainly an unwieldy one. Perhaps a better term should be devised.

Summary

An uncircumcised patient with a persistent penile plaque of one-year duration cleared three times completely with hydrocortisone acetate salve but always developed recurrence in the same area of the glans penis with cessation of therapy.

121 S. Glenoaks Blvd.

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A Simple Portable Dark-Field Microscope

LEON GOLDMAN, M.D., and FAYE SAWYER, Cincinnati

There is still a need in dermatology for dark-field examination of skin lesions. Unless a separate microscope is set up for this, there is often difficulty getting such examinations even by the dermatologists.

Our experience with the staining of spirochetes has shown inconstant results. Our preferred technique at present is still the use of fountain-pen ink, developed in the department by Emura.[1]

Submitted for publication Oct. 15, 1958.

From the Department of Dermatology, University of Cincinnati College of Medicine.

The microscope was obtained from Dr. John McArthur, 101 Chiltern Ct., London N. W. 1.

For the past year, for routine dark-field examinations we have been using the McArthur microscope.[2,3] This special microscope was devised originally for field work in tropical medicine. It has an original design based on a prismatic system. It measures only 4×2½×2 in. and weighs only 18 oz. For dark-field examination we use the dark-field condenser, precentered and prefocused with a built-in electric illuminator. Material is taken in the usual manner from an active lesion. Immediately this slide is put on this simple portable microscope and examined under dark-field illumination. We can pass this portable microscope among student groups in the clinic. We have employed this dark-field illumination with this micro-

The McArthur portable microscope used for dark-field examination.

scope also for the examination of sections of two cases of argyria.

In addition, the microscope with its ordinary lens system can be used as an additional microscope for examining routine pathological material in dermatology.

From our experience, the microscope is a practical instrument. It is a precision instrument and should be handled with care.

Department of Dermatology, Cincinnati General Hospital (29).

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Hula-Hoop Dermatitis

IRVING N. HOLTZMAN, M.D., Brooklyn

The following case report is submitted for the purpose of indicating the dermatologic ramifications of contemporary changes in our social mores.

The patient, a 4-year-old girl, was first seen on Oct. 11, 1958, with a papulovesicular eruption, itching in character and limited to the palms of both hands from the wrists to the fingertips. Its duration, approximately two weeks prior to examination, seemed to coincide with the purchase of a "hula hoop." Clinically, the impression was one of contact dermatitis. She was advised to discontinue the use of the hoop and was given a 1% hydrocortisone cream to apply topically twice daily.

She was seen a week later, with considerable improvement and showing only a residual scaling of the palms. At this time patch tests were performed with scrapings of the plastic material from the surface of three different-colored hoops which she had used. Forty-eight hours later, an erythematous papular reaction was present at all three sites. The child is now using an aluminum hoop; she is very happy, and the eruption has subsided practically completely.

Submitted for publication Nov. 5, 1958.

135 Eastern Pkwy. (38).

Skin Planing

G. H. HOEHN, M.D., San Gabriel, Calif.

One of the hazards of skin planing is to get the wire brush or even the diamond burrs caught in a piece of gauze. In an attempt to avoid this hazard I use sterile Kleenex to mop up while I am planing, and I find that it absorbs blood quickly, and in the event that the brush does contact the Kleenex, only a very minor furor is created.

For years, shavers who use a straight or safety razor have felt that cellulose paper, similar to Kleenex, is efficient in inducing clotting and in stopping bleeding of the little nicks made in shaving. It cuts down the bleeding in planing cases too. However, if it is left on for more than 5 or 10 minutes, it adheres to the skin. It is best to open a 2 in. gauze square to single thickness to lay it against the face first, then to lay the sheets of Kleenex against it as soon as one side is planed. Then the Kleenex will lift off very easily as the gauze is lifted. This process is repeated until the bleeding is fairly well controlled, and then Telfa dressings are applied.

Submitted for publication Nov. 26, 1958.

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206 E. Las Tunas Drive.

Erythema Multiforme (Stevens-Johnson Syndrome) Caused by Penicillin

HOWARD S. YAFFEE, M.D., Cambridge, Mass.

In view of the recent interest in the viral etiology of exudative erythema multiforme[1] with fever and mucosal involvement, it must be remembered that other causes have been ascribed to this condition, which probably represents a nonspecific systemic tissue reaction, either toxic or allergic, to varied causes. Among these are bacteria, drugs, viruses, and toxins.

In the past, some authors were impressed with the specificity of antibiotics as therapeutics of choice,[2,3] but recently steroids have been reported most frequently as successfully effecting a favorable outcome. The case reported is an example in which an antibiotic is the suspected causative agent, the cure attributable to corticotropin (ACTH) administered intravenously.

Report of a Case

A 22-year-old white, single man was admitted to the hospital with the questionable diagnosis of smallpox. His history included exposure to this disease in a town in South America three weeks previous to his admission. Some three weeks later he was seen and admitted for a severe generalized vesiculobullous eruption associated with profound toxemia and fever.

On examination, he was a desperately ill young man, with a temperature of 106 F and stertorous breathing, toxic, and wasted. His mucosal surfaces were serous, mucoid, desquamating, and foul. Over his integumen were numerous macules, papules, plaques, and nodules of erythema; large vesiculobullous areas surrounded with a corona of erythema; so-called iris lesions, and huge bullous lesions. Involvement was noted over the entire skin, including the palms and soles.

He was severely dehydrated, as reflected in his laboratory studies. WBC were 17,000, with 68% polymorphonuclear cells. Hematocrit was 55%. Chest film was normal.

The diagnosis of exudative erythema multiforme (Stevens-Johnson syndrome) was made, and the patient was started on intravenous corticotropin, 80 units over an 8-hour period, with gradual resolution of fever to 104 F in 48 hours and further lysis during the next 3 weeks; the dose was reduced as clinical improvement took place. Oxytetracycline (Terramycin), which had been administered during the first five days of his illness, was continued prophylactically. Intravenous nutrition and careful maintenance of electrolyte and fluid balance further sustained him during the period of his acute illness. His toxemia and desperately ill status abated after 36 hours of corticotropin, although he remained ill for an additional three weeks, recovering without sequellae.

On reconstructing his illness, it was learned that two weeks prior to the onset of his first lesion he suffered an abrasion of the leg, which was treated with penicillin ointment. Five days later he noted slight erythema of the area, followed by an itching, weeping vesicular eruption which spread locally. This was regarded as an infection, and he was treated with intramuscular penicillin. Ten days after his first injection he developed the acute onset of generalized erythema multiforme and high fever, which progressed to the ulcerative mucosal picture and severe toxemia with which he presented.

After his recovery he declined further attempts at allergic investigation with penicillin.

Submitted for publication Oct. 20, 1958.

Summary

A 22-year-old white man with severe exudative erythema multiforme without visceral complications, probably caused by penicillin, recovered completely after treatment with intravenous corticotropin (ACTH).

60 Brattle St. (38).

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Chlorothiazide Drug Eruption Involving Photosensitization

ARTHUR L. NORINS, M.D., Chicago

Chlorothiazide (Diuril) is finding increased use in medicine as a diuretic. It is related to the sulfonamide group of drugs, and, therefore, drug reactions occurring during its administration would not be unexpected. Several cases of drug reactions to chlorothiazide have already been reported.[1,2] Another case is reported herein, one in which, for the first time, light influenced the reaction.

It occurred in a woman of 87 years, seen in Dr. Rattner's practice, who presented a painless nonpruritic eruption, consisting of numerous tiny petechiae confined to the exposed areas of the body. They were much more predominant on the anterior surface of the legs, which had been deliberately exposed to the sun. But most interesting was the striking pattern on the feet, where the eruption affected only the open areas of her shoes, particularly the great toe—she wore open-toe shoes.

She had been taking chlorothiazide for chronic cardiac disease for about two weeks prior to the onset of the eruption. It faded within four weeks after the drug was discontinued.

The peculiar distribution of lesions was due to her custom of sitting on a deck chair and exposing her legs to the sun—hence the involvement of the anterior surfaces.

The sequence of events would indicate that the purpuric eruption in this case was a manifestation of a drug eruption, involving photosensitivity brought on by the use of chlorothiazide. For obvious reasons, the eruption was not deliberately reproduced to prove a point.

104 S. Michigan Ave.

Submitted for publication Sept. 16, 1958.

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Topical Therapy with a New Distilled Bituminous Asphaltite from the Dead Sea

JACOB SHANON, M.D., and SOPHIE KAMNITZER, M.D., Cincinnati

For many years coal, wood, and shale tars have been among the most valuable therapeutic agents in dermatology. As differentiated from these tars, which are classified as pyrogeneous distillates,[1] the subject of this paper is a distilled bituminous asphaltite obtained from the Dead Sea. It was first investigated by the Department of Dermatology, Hadassah University Hospital, Jerusalem, and has been used at that institution for the past 20 years. It was found a valuable therapeutic agent in the treatment of infantile eczema, neurodermatitis, seborrheic dermatitis, and various types of hand dermatoses and helpful in pemphigus, dermatitis herpetiformis, and other pruriginous dermatoses owing to its high antipruritic properties and its nonirritant character. One of us (J. S.) has used this compound for at least 15 years on over 10,000 cases without noting carcinogenic or untoward side-effects.

These experiences stimulated us to do a preliminary critical evaluation of this distilled bituminous asphaltite, in this country, on pruritus

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From the Department of Dermatology, University of Cincinnati College of Medicine. Fellow in Psychosomatic Dermatology, Department of Dermatology and Department of Psychiatry (Dr. Shanon).

and on various dermatoses associated with pruritus. We compared its effect with that of the available tars and with topical steroid therapy. In addition, the patients were observed for possible skin sensitivity and irritation.

Our preferred modes of use were (*a*) 30% bituminous asphaltite (Bitupal)* in a modified zinc oxide ointment and (*b*) 15% bituminous asphaltite in a water-washable cream which could be used as a foundation cream. Two other modes have also been used: (*c*) lotion form of various concentrations and (*d*) the undiluted bituminous asphaltite for direct painting of the skin. This bituminous asphaltite ointment or cream was applied to the affected areas in a thin layer once or twice daily.

Methods of Study

The study was divided into the following stages:

1. Preliminary study of skin sensitivity and skin sensitization. Sixty-three patients with various dermatoses were patch-tested with concentrated bituminous asphaltite, 30% bituminous asphaltite ointment, and 15% bituminous asphaltite cream. After 48 hours, all but two were negative. The patient who reacted with a positive follicular reaction suffered from a contact dermatitis and was sensitive to many forms of topical therapy. The other patient who reacted had multiple sensitivities and showed a positive reaction also to 2% crude coal tar in zinc oxide ointment, 1% ichthyol in zinc oxide ointment, and 8.7% shale oil ointment. An additional 76 patients without dermatoses, from a hospital for chronic diseases (Drake Hospital), were skin-tested in the same manner, with equally negative results. The same tests were repeated on 20 of our patients after several weeks, without any reactions.

2. After these preliminary studies, 85 patients were selected for topical treatment with bituminous asphaltite. The duration of the diseases was from 2 months to 34 years. These patients, ranging in age from 1 to 82 years, were treated with 30% bituminous asphaltite ointment and/or 15% bituminous asphaltite cream. There was no concomitant systemic therapy with antibiotics or with steroids in this entire group. They were studied for a period of three to eight weeks and followed for a period of six months. These 85 patients were divided into three groups: (*a*) 54 patients who had either been treated previously with various tars in different concentrations or other topical therapies or had received no previous treatment; (*b*) 19 patients in whom the results of the bituminous asphaltite therapy were compared with results of 2.5% hydrocortisone ointment; (*c*) 12 patients who were treated simultaneously in symmetrical areas with 8.7% Colorado shale oil ointment and 30% bituminous asphaltite ointment.

The indications included atopic dermatitis; eczematous hand dermatitis; infectious eczematous dermatitis; neurodermatitis; pruritus scroti, ani, and vulvae, and seborrheic dermatitis.

* This was supplied, as Bitupal, by S. Musher, Aveeno Corporation, New York.

Comment

From the results of our study it appears that 30% bituminous asphaltite ointment and 15% bituminous asphaltite cream are very effective in various acute and chronic pruritic dermatoses.

1. Bituminous asphaltite shows a low incidence of skin sensitivity.

2. It has a good healing effect on the skin. In some cases the 30% bituminous asphaltite ointment was too drying. Nevertheless, the patients tolerated it, and no untoward reactions could be observed. In such cases, the 15% bituminous asphaltite cream is indicated, particularly in antecubital areas and regions of the neck and face. The cream is cosmetically acceptable and washed off easily. The odor is not objectionable to many patients.

3. Bituminous asphaltite has a very strong antipruritic effect, which seems to us to be more pronounced than that of many available tar preparations.

4. The reparative and antipruritic effect of bituminous asphaltite was at least as potent as that of 2.5% hydrocortisone ointment; in some cases it proved even more effective.

5. The 30% bituminous asphaltite ointment produced significantly better results than an ointment containing 8.7% Colorado shale oil.

6. Bituminous asphaltite has a low index of skin sensitization. Nevertheless, this medication should be used cautiously in the multiple reactor type of patient.

Summary

A new distilled bituminous asphaltite (Bitupal) from the Dead Sea was studied. Eighty-five patients with various dermatologic disorders were treated in this series, and, in addition, skin sensitization was studied. A critical comparison was made also with the available tars and corticosteroid preparations. Bituminous asphaltite can be considered an effective antipruritic, antieczematous, and anti-inflammatory agent.

Department of Dermatology, Cincinnati General Hospital (29).

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Probable Acrodermatitis Enteropathica Treated with Nystatin (Mycostatin)

CHARLES W. WHITMORE, M.D., Lynchburg, Va.

A 3-month-old Negro boy was first seen, on June 3, 1958, several weeks after a hospitalization by his pediatrician for diarrhea which had been difficult to control. The child continued to have four to five loose stools a day at the time he was seen. The pediatrician had not noted significant dermatitis during the hospitalization. A generalized dermatitis bearing some resemblance to atopic dermatitis was present. Loss of hair in the frontal region of the scalp was very marked. The child was irritable and did not eat or sleep well.

A tentative diagnosis of acrodermatitis enteropathica was made at the time of the first visit. Scrapings from the skin and fecal material were both cultured on Nickerson's medium. Both cultures were positive for candida albicans.

Because therapy with diiodohydroxyquin (Diodoquin) in acrodermatitis enteropathica has tended to be prolonged, although apparently successful, it was decided to treat this child with nystatin. I had previously seen only one case of acrodermatitis enteropathica, and that child was treated successfully with diiodohydroxyquin.

It was felt that this was not a case of generalized cutaneous moniliasis occurring in an infant, cases of which I have previously seen.

The question whether C. albicans involvement of the gastrointestinal tract and of the skin is a secondary phenomenon or represents the primary disease has not been clear in the past.[1] It was felt that by treating with a specific fungicidal preparation without other therapy partial light might be shed on this question.

The child was placed on nystatin for suspension orally, 100,000 units four times daily, and zinc oxide emulsion containing nystatin for suspension was applied topically.

Submitted for publication Sept. 25, 1958.

One week after the initiation of therapy the skin had cleared remarkably. The stools had firmed considerably but were still coming at the rate of four or five a day.

June 26, 1958: The child had shown substantial regrowth of hair; the frequency of bowel movements had reduced to two a day and were formed. Except for an isolated patch or two, the skin seemed very clear. At that time, the topical therapy was changed to nystatin ointment because of excessive drying with the zinc oxide emulsion base. A repeat stool culture was obtained on June 26.

July 3, 1958: Bowel movements continued to take place at the rate of one or two a day and were formed. The child was considerably less irritable. Regrowth of hair continued. The stool culture taken on June 26, was negative.

July 24, 1958: Regrowth of hair was very substantial; the skin was entirely clear; the stools remained solid, with a frequency of one or two a day. The child's appetite was good. The mother noted that this was no longer a fussy baby. An additional stool culture was taken on July 24, which showed no growth when read at three weeks.

Sept. 15, 1958: Reexamination revealed a well baby.

The results in this single case seem to suggest that the primary pathology of acrodermatitis enteropathica might be that of a C. albicans infection. The mechanism by which the alopecia is produced has not been specifically elicited.

214 Langhorne Rd.

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The New, Newer, and Newest

Back home from a restful vacation in sunny California to find that *Time* magazine had ruffled the feathers not only of the good citizens of Bolivia but also of a number of our dermatologists for its none-too-skillful abstract of the article on x-ray damage by those three learned Harvard plastic surgeons, published in the *New England Journal of Medicine* recently. Rather, spleen should be vent against the authors who, under the ingenious title, "Malignant Irradiation for Benign Conditions," ingenuously report 165 cases of roentgen damage, "a number of which have previously been reported by Daland" in 1941. There are illustrations of

—an ulcer resulting from treatment of a plantar wart by a general practitioner;
—the hand of a dentist exposed to x-rays repeatedly over a period of 35 years;
—a man whose port-wine mark on the face was irradiated in infancy;
—a woman's chin damaged by the Tricho method;
—a young man treated "presumably for scrofula;"
—a burn due to fluoroscopy 45 years previously;
—two patients with carcinomas of the face that had been treated for acne 27 and 34 years previously. This last case is the only one attributed to treatment by a dermatologist.

"Patients," they report, "continue to appear with permanent tissue destruction that has resulted from recent radiation," (only the one case cited of plantar wart was "recent") and "it . . . is an increasing problem since twice the number of cases were observed . . . in the decade 1948 to 1957 as in the preceding decade." How penetrating!

The authors admitted failure to determine exact doses of irradiation administered to each patient. Except for one case, they failed also to note whether or not the patients had been treated by dermatologists. And they inaccurately assessed the "optimistic" review of 1,000 cases by Sulzberger et al., which showed radiation atrophy in but 2.8% of cases that had received small weekly doses totalling as much as 1,400 r. The authors comment?—"These patients were followed only for 5 to 23 years. In the present study, the average interval for development of cancer was 28 years." This, in spite of admitting ignorance of the amount of radiation administered to their patients! And the implied portent with regard to Sulzberger's cases is inexcusable. What did these surgeons hope to accomplish? Was sensationalism the object?—then why not a report of malignant or mutilating surgery for benign conditions?

Recently, a letter and reprint of an article on acne by Drs. Schonberg and Litt was circularized by the Gebauer Chemical Company. It was done so without the knowledge or permission of the authors. The firm now apologizes for the incident, and we hope that the apology stems from altruism.

Comes, too, a letter from the Pfizer Laboratory people protesting at length and vehemently against the criticism of them in the article on miracle drugs in the *Saturday Review of Literature* (N-N-N for February), and with the letter—they couldn't resist it—was a booklet extolling their oral hypoglycemic agent.

The note (N-N-N for March) concerning specialty societies that meet on the week-end prior to the A. M. A. convention has stimulated much comment. The facts, I now learn, are these:

Only unofficial feelers have been made regarding the matter of joint meetings, the rumors I heard were only rumors; to effect a joint meeting will take some doing because societies usually have to arrange for meeting places and dates for several years in advance due to the taut situation with respect to meeting halls and hotel rooms. Besides, the officers of the various societies are not empowered to act without sanction from their directors, trustees, or memberships, which meet usually only once a year.

Even though the statement was based on inadequate information, I still think that the present practice should be changed. If the joint meeting cannot be effected, the S. I. D. should meet on the week-end after the A. M. A. convention or at some other time. Let us hope that

the matter will be considered at the forthcoming June meetings. ("The views expressed here are those of the author, not of etc., etc.")

Harry J. Hurley has been appointed Professor and Chairman of the Department of Dermatology at Hahnemann Medical College of Philadelphia.

Maurice M. Tolman has been appointed as acting head of the Department of Dermatology at Harvard Medical School.

The Phi Delta Epsilon Fraternity has established the Dr. Charles Robert Rein fellowship in dermatology at New York University.

Louie A. Brunsting delivered the second Howard Fox Memorial lecture at New York University Post-Graduate Medical School, April 2, 1959.

The Skin and Cancer Hospital of Philadelphia has announced a consulting service in Dermal Pathology with Dr. Elson B. Helwig the consultant.

In Oklahoma, there is a dermatologist whose secretary files correspondence from the ARCHIVES under the letter R.

Sam Allison of Honolulu, in our newest state, suggests a new term—epidermectomy—to replace skin-planing or dermabrasion.

It was in Los Angeles, where I attended a meeting of the Metropolitan Dermatological Society, that I learned:

—J. Walter Wilson addressed the annual clinical conference of my own Chicago Medical Society in March on "The Importance of Fungus Diseases;"

—Molleurus Couperus addressed the ninth annual regional Postgraduate Institute, San Joaquin Valley counties, in March on "Problems in the Treatment of Skin Disorders;"

—Tom Sternberg, in addition to his dermatologic duties, is Assistant Dean for Postgraduate Medical Education at U. C. L. A.;

—Paul Foster has been elected President of the California Medical Association;

—The California Medical Society urges the people of California to look upon their doctors as "health engineers," and "in that capacity to be at your service to assist you in making arrangements for the best medical care on the most reasonable financial basis possible."

Regardless of smog, the members look as if they had found the "never-never land." They appeared youthful, moved and talked with the ease of youth, and they seemed big and healthy in their tiny foreign sportscars.

And it was in a California paper that Stanton May noted the following ad: "Gent with psoriasis, seeks lady with same."

H. R.

Society Transactions

THE CLEVELAND DERMATOLOGICAL SOCIETY

George M. Stroud, M.D., President
John A. Kenney Jr., M.D., Secretary
Robert Gardner, M.D., Reporter

March 27, 1958

Idiopathic Atrophoderma. Presented by Dr. A. F. Piraino.

A 39-year-old white man was seen in my office for the first time on Nov. 4, 1957. He complained of discolored patches on the body of about two years' duration. He had no subjective symptoms. He stated that he had been in the Philippines for about eight months several years ago. He had had no previous therapy.

Examination revealed round and oval, slightly depressed, bluish, violaceous macules especially located on the back, chest, hips, inguinal areas, and proximal portions of the lower extremities. The lesions varied considerably in size, and there is no real atrophy. The deeper vessels seem to be visible. Borders of the lesions are sharply defined, and the skin surrounding the patches is normal in appearance.

Histologic examination of a section from the lower back shows the horny layer to be relatively normal. The rete layer is slightly acanthotic but otherwise not remarkable. The upper corium shows a good deal of homogenization of collagen and scattered perivascular lymphocytic infiltration. The rest of the corium appears to be relatively normal, although there are a few areas again of perivascular inflammation.

Treatment: None.

Discussion

Dr. Ruth R. Rauschkolb: When I was interested in studying the atrophies of the skin, some time ago, I realized how many of them had come to be known by eponyms. The excellent review by Dr. Orlando Canizares et al. on idiopathic atrophoderma, in the January, 1958, issue of the A. M. A. Archives of Dermatology, points up the recognition of the contributions of Pasini and Pierini to this subject. One can well understand the desire to honor and memorialize men who have contributed so much to identifying these entities. Yet the fact remains that eponymic names are a little harder to remember, and there always remains the question of whether the various varieties of skin atrophies really constitute specific entities.

In consideration of atrophoderma maculatum, the dermatosis, named by Jadassohn anetoderma erythematodes, has come to be known as Jadassohn's anetoderma. Acrodermatitis atrophicans chronica has pretty well superseded its synonym, erythromelia of Pick-Herxheimer. Multiple benign tumor-like growth has not done as well in pushing aside the designation Schweninger-Buzzi disease.

Lester Hollander et al., in the 1942 Archives of Dermatology described the occurrence of four different types of skin atrophy in a single patient, a Slavish white laborer. This patient exhibited acrodermatitis atrophicans chronica on his lower extremities, Schweninger-Buzzi disease on the back of his torso, Jadassohn's anetoderma, and subcutaneous atrophy.

Workers in this field have felt the various entities could be differentiated on the presence or absence of erythema at the onset of the dermatosis, the pliability of the skin, the location and color of the lesion, and above all the histopathological examination. The field of skin atrophies remains a very fertile one for investigation.

I suppose I should have thought of scleroderma first if I had seen this man as a patient.

Dr. Richard B. Stoughton: I was impressed with the possibility that these could be lesions of morphea. It is not typical, but there is enough induration and depression of the skin in this area. The histologic picture is a little more in favor of morphea than one of the atrophodermas.

Dr. George W. Binkley: Idiopathic atrophoderma of Pasini and Pierini has been presented by Canizares, Sachs, Jaimovich, and Torres. (A. M. A. Arch. Dermat. 77:42 [Jan.] 1958.)

In this study, they traced this peculiar cutaneous atrophy back to Pasini in 1923. There are good reasons to set this atrophy apart from scleroderma and others because of the good prognosis. The process is more or less self-limited and is not accompanied by systemic involvement, such as esophageal or gastrointestinal atrophy.

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DR. A. F. PIRAINO: I think probably there are two types of cases included. One is the type that approaches the morphea type and the progressive idiopathic atrophoderma, according to the recent literature on it. As far as therapy is concerned, I have not used anything on this man and I guess there is nothing to do for him. As you mentioned, leprosy was the question somebody asked about, but of course there is no evidence, either histologically or clinically.

Widespread Eruption Due to Trichophyton Rubrum. Presented by DR. G. M. STROUD.

Granuloma Annulare. Presented by DR. GERARD A. DEOREO.

Telangiectasia, Hereditary Hemorrhagic (Osler-Rendu-Weber). Presented by DR. GERARD A. DEOREO.

Telangiectasia, Hereditary Hemorrhagic (Osler-Rendu-Weber). Presented by DR. GERARD A. DEOREO (Courtesy of George Gabuzda, Jr., M.D., Department of Medicine, Western Reserve University.)

Vitiligo. Presented by DR. JOHN A. KENNEY, JR.

Pemphigus Erythematodes. Presented by DR. T. SZOLAMAJER and DR. D. SEVASTIANOS, Department of Dermatology, Cuyahoga County Hospital, Service of Dr. Ruth R. Rauschkolb.

Spindle Cell Nevus (Juvenile Melanoma). Presented by DR. RUTH R. RAUSCHKOLB.

Vitiligo. Presented by DR. JOHN A. KENNEY, JR.

Unusual Case of Multiple Basal Cell Epitheliomas. Presented by DR. JOSEPH C. AMERSBACH (by invitation).

Tissue Electrolyte Changes in Anaphylactic Shock. Presented by DR. C. T. NELSON, Department of Dermatology, Columbia University College of Physicians and Surgeons.

Perifolliculitis Capitis Abscedens et Suffodiens (Dissecting Cellulitis of the Scalp). Successfully Treated by X-Ray Epilation. Presented by DR. JOHN A. KENNEY, JR.

THE CLEVELAND DERMATOLOGICAL SOCIETY

April 24, 1958

Some Unusual Forms of Cutaneous Moniliasis.

Presented by DR. STEPHEN ROTHMAN, The University of Chicago.

I shall discuss monilial granuloma and acrodermatitis enteropathica. But before I do so, I would like to say a few words about the picture of the not quite unusual generalized cutaneous and systemic type of moniliasis.

It is pretty much a valid axiom that if Candida albicans settles on dry, nonintertriginous skin and causes rapidly spreading lesions one has to look for some systemic factor which substantially increased the susceptibility of the skin to the pathogenic effect of C. albicans. In other words, in cases of thrush or monilial perleche or interdigital moniliasis or in moniliasis of the large folds the local suspectibility factor of continuous moisture suffices in most cases to explain the pathogenesis.

The commonest systemic susceptibility factor, of course, is diabetes. But even in diabetes, particularly in obese women, monilial infection can remain restricted to the large folds. If the disease spreads to nonintertriginous areas, this always indicates an extraordinary and usually grave situation.

I should like to illustrate this by telling you about a case which I observed, together with Dr. Beckersen and Dr. Kahn, back in 1941 (ARCH. DERMAT. & SYPH. 45:1069-1080, 1942). This was the case of a 45-year-old woman who had a widespread eruption in symmetrical distribution for eight months prior to admission. She had lost 17 lb. during this period and had noticed increasing weakness for several months. There were papulovesicular and crusted lesions of the face and perleche, and I may add that her tongue also was involved. There were widespread and confluent patches of superficial necrosis. These lesions developed and spread with frightening rapidity under our eyes, and when new looked like carbolic acid burns. There also were purpuric elements.

Candida albicans was cultured from under the nails and from all skin and mouth lesions. At that time the only available antimonilial remedy was gentian violet. While single lesions responded very well to this application, new lesions came up with frightening rapidity, and the patient took a rapid downhill course.

Laboratory tests yielded one flat glucose-tolerance curve but on repetition a diabetic curve—and we were inclined to blame the laboratory for some error. However, when the patient died with an acute thrombosis of the left iliac vein and in peripheral vascular collapse, the autopsy revealed an islet-cell type of pancreatic carcinoma. Apparently this tumor produced intermittently more or less insulin, so as to induce a flat curve on one occasion but permit a diabetic curve to break through on another occasion.

In spite of the unusual cause and unusual course of the disease, the C. albicans did not cause any unusual reaction on the skin or mucous membranes. It only caused what it always does in banal cases, namely, liquefaction necrosis in the epithelial cells, with reactive superficial inflammation.

In monilial granuloma the situation is different. As the name indicates, in patients afflicted with this disease the reaction to the invasion by Candida is a dense infiltrate, consisting of lymphocytes, plasma cells, polymorphonuclear leukocytes, and foreign-body giant cells, and I may add that this infiltrate

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extends down to the subdermis. I also want to emphasize that C. albicans, with all its characteristic mycological properties and with its animal toxicity, can be cultured from *all* the lesions without exception with great ease and even from their deep layers, although it cannot be recovered from uninvolved skin. No other fungal organism is ever found. Therefore, I cannot understand why it is doubted by some authors, such as Benedek, that C. albicans plays a causative role in the pathogenesis of these lesions. We dug out a case from the literature, where the attending nurse was infected by the child's lesion and thus acquired a trivial typical monilial interdigital erosion. This proves to me sufficiently that the fault in monilial granuloma lies with an abnormal reaction of the host to the organism.

I show you the slides of our first case, which you may remember from our publication. The monstrosity of the picture was caused mainly by the multiple horn formations, as have been reported also by others. Actually, these horns consisted of a mixture of keratin and crusts.

In connection with this case we uncovered 13 case reports, strikingly similar to our case in all respects. In many cases the picture of the scalp, face, and nails nearly duplicated ours. The next slide shows a photograph taken from MacKee and Cipollaro's book on skin diseases of children. It had the caption "Moniliasis."

In studying these cases in the literature, we found that in this disease the age of onset is in early childhood, mostly before the fifth year of life, although more recently some adult cases were reported. There is no sexual predisposition. In no case was the infection acquired or transmitted to other persons in this form. The prognosis for life seems to be poor, the patients dying in early youth.

For several years our patient had no findings indicating systemic disease, except that C. albicans was cultured not only from the skin, appendages, and the mouth but also from saliva and stools. His glucose tolerance test was normal on repeated examination. However, in the third year of observation he was brought in in diabetic coma, which developed very suddenly. Later, the child died in Cook County Hospital, having severe diabetes. Unfortunately no permission for autopsy was given.

I had the opportunity to see a second case sent to me for consultation. This child was seen previously at the Mayo Clinic, where pancreatic fibrosis was suspected. We were able to perform a modern pancreatic-function test on this child, namely, the administration by mouth of protein which was iodinated with I^{131}. In case of insufficiency of external pancreatic secretion, this protein is insufficiently digested (hydrolyzed), and in the urine the radioactive material will not be excreted or will be excreted in diminished quantities. This test showed seriously impaired pancreatic function in this child.

With the first child dying with diabetes and the second also having pancreatic disease, I have little doubt that some kind of pancreatic disease is the basis for this tragic, hitherto intractable disease.

Mycostatin (Nystatin) was discovered and became available before our first patient died. It was given locally and by mouth, in Cook County Hospital. The child's lesions improved locally, but the cultures continued to be positive.

We have a rosier picture in another disease, acrodermatitis enteropathica, because it now has a successful treatment method.

This disease had been described since 1902 under varied names, such as atypical epidermolysis bullosa (Wende), atypical acrodermatitis continua of Hallopeau, systemic thrush, moniliasis, unusual syndrome with C. albicans infection, etc., until, in 1942, Danbolt and Closs recognized its clearly distinctive features and gave it its present name.

This is a mostly fatal disease of early childhood, prominently attacking the skin and gastrointestinal tract. It mostly commences in infancy, often at the time of weaning from the breast, and runs an intermittent yet progressive course, often ending in death during childhood from general debility and intercurrent infection. There is a definite tendency to familial occurrence, and several data suggest that it is a recessively inherited abnormality.

The cutaneous manifestations appear as fairly well-defined, roughly symmetrical patches, located around the mucocutaneous orifices and on the extremities, especially distally and around the elbows and knees. Early the lesions are vesiculobullous, but later they often become pustular and even psoriasiform. There are severe paronychias and dystrophic nail changes. Alopecia of the scalp, eyebrows, and eyelashes is characteristic and progresses, especially during periods of disease activity. During the exacerbations there is a diarrhea and abdominal discomfort, coupled with a mental attitude of abject, literally head-hung misery, as Lorincz has expressed it. There is also a stunting of growth, but intelligence is not affected.

The skin lesions are frequently infected with C. albicans but, in contrast to monilial granuloma, not always. In some cases no C. albicans could be demonstrated in any of the lesions. This, of course, puts the disease in a different category from generalized moniliasis and monilial granuloma, insofar as here the skin lesions are not primarily elicited by monilial infection. Apparent elimination by therapy of C. albicans from the lesions fails to alter the course of the disease.

Still, it is obvious that the basic disease creates an extremely high susceptibility to monilial infection of skin and mucous membranes. Thrush is found in most cases. The basic disturbance, however, seems to reside in the gastrointestinal tract.

The gastrointestinal symptoms and diarrhea, coupled with the psychic manifestations, increased suspectibility to infection, retarded growth, onset during the first weeks or months of life, often at the time of weaning, and intermittent progression, mostly ending in death during childhood, are all reminiscent of the celiac syndrome of the pediatrician and of pancreatic fibrocystic disease (which actually was discovered at autopsy in a case of acrodermatitis enteropathica, by Ugland).

In the celiac syndromes there is faulty absorption of nutrients from the intestinal tracts, either because of inadequate secretion of pancreatic juice, with actual disease of the pancreas, or because of some primary defect in the intestinal absorptive mechanism, as in the so-called idiopathic celiac disease. Human milk apparently contains some enzymatic or other factors that help compensate the faulty absorption in either case.

There are findings in acrodermatitis enteropathica which make it difficult to identify it with the celiac syndrome, such as frequent absence of fat and starch in the stools, absence of demonstrable lipase and amylase deficiency in the bowels, and absence of hypochromic anemia and abnormal glucose tolerance tests. Still, the similarities are remarkable, and only further studies will clear the relationship of the two abnormalities.

It is most interesting that Giardia lamblia infestation was found in two cases of acrodermatitis enteropathica. G. lamblia is generally considered nonpathogenic, but there are scattered reports on findings of giardiasis underlying some celiac-like syndrome.

We became involved in acrodermatitis enteropathica when we had a case which was originally diagnosed as dystrophic epidermolysis bullosa. The correct diagnosis of this case was made by Hermann Pinkus, in the Chicago Dermatological Society. As a fortuitous accident, it happened that at that time our department was visited by a general practitioner, Dr. Schlomovitz, who most enthusiastically and passionately claimed that generalized moniliasis can be cured by the administration of Diodoquin (diiodohydroxyquin). Several prominent dermatologists in Chicago knew about Dr. Schlomovitz's claim and assured us that Dr. Schlomovitz was mistaken. But when our little patient went from bad to worse and it looked like the end was not too far away, we tried Diodoquin, 210 mg. q. i. d. Within four days there was striking improvement, and complete remission was achieved in a few weeks. This was in 1952, and ever since the child has been well with the possible exception of very occasional marginal blepharitis, which promptly clears after the administration of Diodoquin for a day or two.

We know of more than a dozen additional cases in which Diodoquin has proved to be effective. Sometimes the results are not as strikingly rapid and complete as in our case. More or less continuous therapy is required, sometimes at higher dosages, to achieve and maintain improvement. Cure is not always complete.

Incontinentia Pigmenti (Bloch - Sulzberger), Early Stage. Presented by Dr. Richard B. Stoughton and Dr. W. P. Lascheid.

A 7-week-old infant was first seen by Dr. Anthony Piraino at birth and referred to University Hospitals at the age of 3 weeks, with the diagnosis of incontinentia pigmenti.

The infant was born at term after a normal gestation. The birth weight was 6 lb. 14 oz. The mother had had no unusual medications during her pregnancy. Two siblings are living and well. The mother and father are living and well.

On the day after the delivery, an eruption was noted on the infant's right knee. This was noted as erythema plus blistering. The eruption progressed fairly rapidly to involve all extremities, trunk, and scalp.

Physical examination revealed an alert, active child, with no abnormalities other than her skin eruption, which consisted of vesicles on an erythematous base, arranged in linear streaks and swirls over the extremities, trunk, and scalp.

Urinalysis was negative; S. T. S., negative; hemoglobin, 22 gm.; white blood cell count 29,000, with a differential count showing polymorphonuclears, 14; lymphs, 38; eosinophils, 46, and basophils, 2. X-ray bone survey revealed no abnormalities.

A biopsy specimen of one of the lesions reveals spongiosis and vesicle formation in the epidermis. The vesicle is packed with eosinophils. Eosinophils are noted throughout the upper corium and epidermis in large numbers.

This is consistent with the diagnosis of incontinentia pigmenti, early stage.

Incontinentia Pigmenti (Bloch - Sulzberger), Late Stage. Presented by Dr. Richard B. Stoughton, W. P. Lascheid, and Dr. Sam Sato, Department of Dermatology, University Hospitals.

A 2½-year-old white girl was first seen at University Hospitals on Jan. 5, 1956, having been referred by Dr. Sam Sato with the diagnosis of incontinentia pigmenti. She had been born three weeks prior to admission, following a normal term pregnancy. The birth weight was 7 lb. 2 oz. She apparently reacted normally at birth and was normal, with the exception of her eruption, which was noted as redness and blisters "all over the body" but mostly concentrated in the groin and on the legs. The family history was essentially negative. Venereal disease was denied. During her pregnancy the child's mother had had no infection or

medication. Prior to the pregnancy she had a cystitis, which was treated with sulfonamide drugs.

Physical examination in January, 1956, revealed a 3-week-old normal infant, with the exception of the eruption, which consisted of erythema, arranged somewhat in streaks and swirls, with multiple vesicles distributed over the trunk, extremities, face, and scalp. A few hyperkeratotic lesions were noted, particularly on the extremities.

Urinalysis was negative; hemoglobin, 19 gm.; white blood cells, 29,900, with 20% polymorphonuclears, 31% lymphocytes, and 49% eosinophils. Bone marrow aspiration was reported to be within normal limits. X-ray of bones revealed no abnormalities.

Prior to admission, steroids had been tried, with no response of the lesions. Diodoquin was administered, 50 mg. b. i. d. for one week. No appreciable difference in the eruption was noted.

A biopsy specimen of the early (vesicle) stage revealed an intraepidermal vesicle containing numerous eosinophils. The epidermis shows slight spongiosis, with slight broadening of the rete pegs. There are scattered eosinophils and lymphocytes in the dermis. This is consistent with the diagnosis of incontinentia pigmenti, early stage.

A biopsy of the hyperkeratotic lesion reveals a small verrucous lesion with hyperkeratosis, acanthosis, and minimal focal parakeratosis. Eosinophils and lymphocytes are noted in the superficial dermis. This is consistent with the diagnosis of incontinentia pigmenti, intermediate stage.

Since discharge from the hospital, this child has been followed at intervals by Dr. Sato. A minimal amount of pigment was laid down after the initial lesions disappeared. No other abnormalities have been noted in this child.

Discussion

Dr. W. P. Lascheid: These two cases were presented to show the various stages of the disease. This condition was first described by Bloch, in 1926, and later by Bloch and Sulzberger, in 1928. They described the third stage, a pigmented stage in which the pigment is laid down in streaks and swirls, without any tendency to go along skin lines and without following any nerve roots. In 1951, Carney reviewed the literature and reported five cases of his own, where he pointed out that about 30% of the time this eruption is preceded by an erythematous, vesicular eruption and again about 30% of the time by hyperkeratotic lesions. He also pointed out that this disease is frequently associated with other abnormalities, such as cataracts, delayed dentition, mental retardation, etc.

We wanted to present these two cases to show primarily the vesicular stage and the hyperkeratotic lesions in the first case and the laying down of the pigment in the second case.

Dr. Richard B. Stoughton: I think it is interesting to note the large number of eosinophils in the early stage and also that there is a peripheral eosinophilia in association. I should like to mention some of the work we have done. We have taken normal human epidermis and made extracts after proteolysis. This extract, when injected into normal skin, results in the attraction of 20% - 50% eosinophils to the area. This probably explains the tissue eosinophilia we see associated with many epidermal lesions.

Angiokeratoma Corporis Diffusum (Fabry). Presented by Dr. Richard B. Stoughton and Dr. W. E. Clendenning.

A 48-year-old white man was admitted to University Hospitals for the third time on July 24, 1957, with the complaint of dizziness, accompanied by nausea and vomiting, of one month's duration. The vertigo was described as intermittent and seemed associated with lying on the left side. He also gave a history of tinnitus and loss of hearing. As long as he can remember his skin has appeared as it does at present. There have been no symptoms referable to the skin.

The patient had osteomyelitis of the right tibia in 1940. He had had two previous admissions to University Hospitals, in 1954 and 1955, for an unexplained albuminuria. After an extensive work-up, no abnormalities were revealed other than benign prostatic hypertrophy.

On physical examination the blood pressure was 155/105. There was rotary nystagmus on right lateral gaze. The prostate was enlarged times two. The reflexes were hypoactive. The eruption on the skin was mainly confined to the trunk and was more prominent on the lower aspects, particularly the buttocks. It consisted of small, 1 to 3 mm., spots and slightly elevated papules, which varied in color from red to brown. They did not blanch on diascopic pressure. The skin in the more markedly affected area was rough.

Urinalysis revealed specific gravity, 1.019; albumin, 2+ and 3+; white blood cells, 2 to 3 per high-power field; casts, 8 to 10 hyaline and finely granular; hemograms, normal; chemistries, normal; urea clearance, 94%; urine culture, no growth; orthostatic albumin test, negative. Electrocardiogram showed incomplete right bundle-branch block and left ventricular hypertrophy. X-rays of the lungs, right tibia, paranasal sinuses, and skull were negative. Two intravenous pyelograms, done on previous admissions, were normal. Caloric testing was normal.

A punch biopsy was taken from the right buttock. The epidermis was normal. In the upper dermis were numerous vascular spaces of varying size, many of them filled with red cells and lined by a single layer of endothelium. A mild chronic inflammatory reaction was present in the upper

dermis. This is consistent with the diagnosis of angiokeratoma.

It was felt by the neurological consultants that the vertigo was on the basis of hydrops of the labyrinth. The patient was given meclizine (Bonamine) hydrochloride, 0/025 t. i. d., with subsequent disappearance of his symptoms. He has remained in good health until the present time. The albuminuria remains unexplained.

Discussion

DR. EARL W. NETHERTON: I am very much interested in this patient, because several years ago I presented a case of this particular entity. There were very many more lesions than this man has. He also had a numbness of one arm, which went on for a long while. Eventually he developed an amblyopia. He had a vascular accident about 10 years after we had shown him. Angiokeratoma was discussed at that time. There is no keratoma that I can see. If we hold with Dr. Weil's original concept, we cannot classify this in that category. This man has many more, some in the mucous membranes. Our patient had lesions in the mucous membranes also, but we did not think it belonged to the hereditary type of disease. Our patient also continued to develop more lesions as time went on. How long have you observed this patient, and has he continued to develop newer small vesicular lesions?

DR. W. E. CLENDENNING: I should first like to answer Dr. Netherton's question. We first saw this patient in August, 1957. During the past nine months there has been no change in the appearance of the lesions.

Angiokeratoma corporis diffusum was first described by Fabry, in 1898, under the name "purpura hemorrhagica nodularis." Over the succeeding 50 years only about 20 cases were described, all in the European literature. Interest has been focused on this entity in the past decade by Ruiter and his associates, who have drawn attention to the systemic and possible familial nature of the disorder.

They have noted what they term a cardiovascular-renal symptom complex in association with the skin manifestations. This consists of (1) vasomotor disturbances, such as rheumatoid pains, cramps, and paresthesias of the extremities; (2) edema of the lower extremities; (3) moderate elevations of blood pressure; (4) cardiac enlargement, particularly left ventricular, and (5) persistent abnormalities of urine, albuminuria, red blood cells, white blood cells, and casts in the sediment.

The opportunity arose to autopsy a case. The essentials of the pathological investigation were thickening of the media of the blood vessels, as the result of accumulation of hyaline material between the muscle fibers, and hypertrophy and pronounced vacuolation of the cytoplasm of the muscle fibers themselves. Scribe, in 1950, demonstrated that the vacuolation of these cells was due to a lipid substance similar to, but not identical with, sphingomyelin.

On the basis of these findings, the investigators postulated a hitherto unrecognized lipoid storage disease as the basic abnormality in this syndrome. Two cases, subsequently reported in the American literature, have demonstrated a similar clinical and pathological picture.

It is of interest that this patient has a brother who supposedly has albuminuria. We would, of course, be most interested in seeing this sibling, but, thus far, neither we nor the urologists have been successful in persuading him to come in. Two of Ruiter's cases were brothers.

A Case for Diagnosis. (Mycosis Fungoides?). Presented by DR. J. R. DRIVER, DR. W. E. CLENDENNING, and DR. SAM SATO.

Pretibial Myxedema. Presented by DR. RICHARD B. STOUGHTON, and DR. W. P. LASCHEID, Department of Dermatology, University Hospitals

Herpes Zoster in Twenty-Month-Old Infant. Presented by DR. HAROLD N. COLE JR.

Solitary Lesion of Urticaria Pigmentosa. Presented by DR. ANTHONY PIRAINO.

Urticaria Pigmentosa. Presented by DR. RICHARD B. STOUGHTON.

Epiloia (Adenoma Sebaceum). Presented by DR. RICHARD B. STOUGHTON and DR. W. P. LASCHEID.

A Case for Diagnosis (Neurotic Excoriations?). Presented by DR. GEORGE M. STROUD and DR. W. E. CLENDENNING.

Scleroderma with Raynaud's Phenomenon. Presented by DR. RICHARD B. STOUGHTON and DR. L. POTTS, Department of Dermatology, University Hospitals.

Scleredema Adultorum (Buschke). Presented by DR. RICHARD B. STOUGHTON and DR. W. E. CLENDENNING.

Hailey and Hailey Disease (Familial Benign Chronic Pemphigus). Presented by DR. JAMES H. MCCREARY.

Multiple Myeloma with Secondary Amyloidosis. Presented by DR. RICHARD B. STOUGHTON and DR. W. P. LASCHEID.

Discoid Lupus Erythematosus. Presented by DR. RICHARD B. STOUGHTON and DR. W. P. LASCHEID.

A Case for Diagnosis (Xeroderma Pigmentosa (Forme Fruste)?). Presented by DR. RICHARD B. STOUGHTON and DR. L. POTTS, Department of Dermatology, University Hospitals.

MANHATTAN DERMATOLOGICAL SOCIETY

Paul Gross, M.D., President
Maurice J. Costello, M.D., Secretary

Feb. 11, 1958

A Case for Diagnosis and Suggestions for Treatment (Erythema Multiforme? Dermatitis Herpetiformis?). Presented by DR. MAURICE J. COSTELLO.

A girl aged 18 months has had a generalized, pruritic eruption of almost four months' duration. The mother is allergic to penicillin; she had one episode of urticaria after the birth of a child three years ago and what sounds like angioneurotic edema 10 years ago, which lasted for one month.

The patient was normal at birth, but at the age of 2 months she had infected tonsils which responded to the mycins. An otolaryngologist felt that the tonsils should be removed but that she was too young. They have been normal ever since. In October, the patient was given a "flu" shot, and 10 days later an urticarial eruption developed. Her pediatrician prescribed elixir of pyribenzamine, but there was no improvement. The urticarial lesions began to form circles and half-circles, and three weeks after the onset vesicles began to appear. There was no history of taking drugs or laxatives except vitamins and iron, which were discontinued without change in the eruption. The patient had been sleeping in a room in which there was a mildewed carpet. She was kept out of it, without improvement. To rule out food allergies the child was given only milk for three days, but there was no change. Her stools were found negative for ova and parasites. On Dec. 4, a urinalysis was normal. Her blood cell count showed hemoglobin, 10.7 gm.; red blood cells, 4,500,000, and white blood cells, 6,200, with 35% polymorphonuclear cells, 59% lymphocytes, 2% eosinophils, and 4% monocytes.

The patient was given elixir of Benadryl and tetracycline and then erythromycin, without improvement. Steroid therapy (4 to 8 mg. of Meticorten daily) produced some improvement and alleviation of the pruritus, but when it was discontinued the eruption and the itching reappeared in full force.

At this point, the child was reexamined by her pediatrician and no abnormalities were found except the eruption. The child was seen then by another dermatologist in consultation, and steroids were discontinued because of the lack of response; she was again given Tetrabon, 1 teaspoonful t. i. d. There was some improvement, but new lesions continued to appear. After two weeks without any real change the antibiotic was discontinued, and the patient has been taking elixir pyribenzamine only p. r. n. for the pruritus.

There has been no essential change in the eruption; vesicles and bullae, occasionally hemorrhagic, continue to appear, as well as the urticarial gyrate lesions. These seem to come in showers about every 10 days.

Urinalysis, on Jan. 27, 1958, was completely normal. On the same day the hemoglobin was 11.1 gm.; red blood cells, 4,300,000; white blood cells, 8,050, with 38% polymorphonuclear neutrophils, 1% band forms, 52% lymphocytes, 3% monocytes, and 6% eosinophils.

Biopsy, on Jan. 27, 1958, showed a subepidermal bulla with a thin, flattened roof. The underlying corium presented superficial, dilated, congested vessels surrounded by a moderate, nonspecific cellular reaction. The diagnosis was erythema multiforme bullosum.

At this time the child was seen in consultation with another dermatologist, and it was felt that the eruption was an erythema multiforme type of dermatitis herpetiformis. As a therapeutic test the child was given 1 Promacetin tablet three times daily. Treatment began on Dec. 23, and by Dec. 28, the urticarial lesions had all but disappeared, but new vesicles were still forming. Examination of the blood, on Dec. 28, showed hemoglobin, 9.7 gm.; red blood cells, 3,970,000, and white blood cells, 6,400, with 38% polymorphonuclear neutrophils, 11% band forms, 47% lymphocytes, 2% eosinophils, 1% basophils, and 1% monocytes. The mother failed to get a urine specimen for examination.

Two days later, despite continuation of the Promacetin, new urticarial lesions appeared and the child was given 4 tablets of Promacetin daily. On the second day after the dosage was increased, the patient became febrile and listless, and the face and eyelids became puffy. The Promacetin was discontinued, and the patient was given 3 mg. of Meticorten. The next morning the fever and swelling were gone, and the child began acting normally. The blood cell count that day showed hemoglobin, 9.7 gm.; red blood cells, 3,400,000, white blood cells, 4,750, and 42% polymorphonuclear neutrophils, 5% band forms, 49% lymphocytes, and 4% monocytes. There was slight hypochromia and occasional poikilocytosis and anisocytosis. Examination of the urine was entirely normal. Steroid therapy was continued and increased up to 15 mg. of Meticorten daily, with no improvement.

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Discussion

DR. NATHAN SOBEL: It would be interesting to speculate what the injection of flu vaccine had to do with this eruption. I think the vaccine contains some antiseptic, which may have been a factor in causing the erythema multiforme.

DR. WILBERT SACHS: The flu injection was given four months ago. Do you think that could have anything to do with the eruption seen today? I think the patient has dermatitis herpetiformis with erythema multiforme, which is not uncommon. I agree with the pathologist; there is a bullous lesion and groups of polymorphonuclear cells, even the papillary bodies. The pathology is that of erythema multiforme underlying dermatitis herpetiformis. I do not think the injection had anything to do with it.

DR. MAURICE J. COSTELLO: When I first saw the patient I was under the impression that the nearest diagnosis clinically was dermatitis herpetiformis because of the urticarial, bullous eruption and the sites of localization, but the eruption did not respond to Promacetin therapy. This is the second time I have seen Promacetin give indication of depressing the blood-forming organs.

DR. SEYMOUR FRIED (by invitation): The man who examined the biopsy specimen thought it was just erythema multiforme, with no evidence of dermatitis herpetiformis. I should like to ask what the consensus is—whether it is more in favor of dermatitis herpetiformis or erythema multiforme. If it is dermatitis herpetiformis, shall we try sulfapyridine? One type of sulfone may work, while another may not.

DR. WILBERT SACHS: I have never seen a pure erythema multiforme with collections of eosinophils in the cutis and in the papillary bodies. That is more significant of dermatitis herpetiformis.

DR. ADRIAN BRODEY: Did this respond to corticosteroids?

DR. SEYMOUR FRIED (by invitation): The first time it was tried there was slight improvement. The second time we gave tremendous doses, up to 15 mg. daily, of Meticorten, which is a very large dose for a child weighing 20 lb., and there was no improvement at all.

DR. MAURICE J. COSTELLO: For a short time (two weeks) it might not be wrong to give Fowler's solution, which has long been known to be helpful in dermatitis herpetiformis, but I would not suggest that it be given for a longer period. Since she had such a bad reaction to Promacetin, I would be very much against giving sulfapyridine. Usually dermatitis herpetiformis does not last long in children. It is either cured after a relatively short period, or it clears up spontaneously.

Infantile Acne. Presented by DR. MAURICE J. COSTELLO.

An 11-month-old baby boy has had facial acne of moderate severity for the past four months, consisting of few comedones, papules, pustules, and scars. Treatment has consisted of resorcinol-sulfur lotion, Ilotycin ointment, and 0.9 cc. of vitamin A daily (equal to 4,000 units), administered in an alternating manner.

Discussion

DR. DAVID BLOOM: Although the acne lesions are bilateral one may consider it a follicular or comedo nevus (analogous to a systematized nevus). It is known that these lesions may be followed by atrophy, as seen in this child.

DR. PAUL GROSS: The child is 11 months old, which is well beyond the age when true infantile acne manifests itself. Therefore, further observation is indicated to rule out endocrine disturbance. Certainly we are not dealing with a nevus comedonicus, which is always unilateral and usually located on the trunk. Atrophoderma vermicularis is not preceded by acneform lesions, and therefore that diagnosis is improbable.

A Case for Diagnosis (Dermatitis Herpetiformis?). Presented by DR. ADRIAN BRODEY.

An 11-year-old girl was previously presented to this society on Nov. 12, 1957, with a complaint of a purpuric bullous eruption of over three years' duration. The patient had responded well to corticosteroid or sulfapyridine therapy, but mild leukopenia had followed use of the latter drug. Biopsy examination, on Nov. 20, showed evidence of a pronounced infection with superficial impetiginization. The picture was that of ecthyma. There was no evidence of extracellular cholesterosis. The γ-globulin fraction was normal. Antistreptolysin titer studies were normal, and bacteriological cultures were negative. Corticosteroid therapy was discontinued, and exacerbation followed, which was dramatically controlled by an initial dose of 4 gm. of Promacetin daily and 2 gm. daily thereafter. This therapy began on Dec. 9, 1957, and on Dec. 21 the while blood cell count was 5,600 with 44% polymorphonuclear neutrophils. On Nov. 18, while blood cell count had been 14,300, with 61% polymorphonuclear neutrophils. On Jan. 7, 1958, the white blood cell count was 2,600, with 27% polymorphonuclear neutrophils, and the Promacetin then was immediately discontinued. On Jan. 13, the white blood cell count was 6,400, with 47% polymorphonuclear cells. The lesions began to recur, and the patient was given 5 mg. of Meticorten three times a day (the maintenance dose), and Mysteclin V, 250 mg. t. i. d. Two weeks later the white blood cell count was 3,500, with 34% polymorphonuclear

leukocytes. All medication was then interdicted. Five days later the white blood cell count had risen to 6,500 and the polymorphonuclears to 46%. The erythrocyte sedimentation rate has been normal throughout. At present the patient presents purpuric vesicular, aggregated lesions over the lower extremities.

Discussion

DR. JOHN W. DOUGHERTY: For what it is worth, I should like to add the possibility of epidermolysis bullosa and Ehlers-Danlos syndrome, neither of which would be complete by any means. I would go along with a diagnosis of dermatitis herpetiformis, in this girl. When she was presented before I did not think much of the leukopenia, but now I have great respect for it.

DR. PERRY SACHS: When I first saw the patient I was impressed by the tremendous amount of infection and ulceration. Today the eruption has a nodular appearance. I think it was the second biopsy specimen, which showed a tremendous infection; the cutis was filled with polymorphonuclear cells, which in itself would rule out the possibility of epidermolysis bullosa. The microscopic picture did not suggest it or extracellular cholesterosis, which was also mentioned at the earlier meeting. However, on biopsy it was impossible to establish a diagnosis of dermatitis herpetiformis. There was pronounced infection, such as an ecthymatous process. While I do not think it is dermatitis herpetiformis, I cannot make a diagnosis.

DR. WILBERT SACHS: Some of the lesions were indurated, and I do not believe biopsy was out of order at all. There may be a reason for the tremendous infiltration of polymophonuclear cells, which suggested ecthyma. I would have thought of something in the nature of acne varioliformis. I wonder if it is not some form of tuberculid.

DR. DAVID BLOOM: I am unable to make a definite diagnosis but wish to state that I too am impressed with the bad scars, which resemble the scars and pseudotumors seen in Ehlers-Danlos syndrome owing to capillary and cutaneous fragility.

DR. MAURICE J. COSTELLO: The most unusual feature of this eruption—and one that is unique to me—is the ecthymatous element. When Dr. Brodey presented the patient last time, I thought it was not Duhring's disease because it responded favorably to steroid therapy, and I have never seen ecthymatous lesions in dermatitis herpetiformis. However, they may represent a super imposed infection. For that reason I suggested to Dr. Brodey that he do γ-globulin determinations. Promacetin may cause leukopenia, and one must keep that in mind. In this case, leukopenia appeared when Promacetin was administered.

DR. PAUL GROSS: I am still more in favor of extracellular cholesterosis than I was when the patient was presented last time. The evolution of the typical lesions of this disease is rather slow, but some of the tumor-like lesions seen today may give a more convincing biopsy result.

DR. ADRIAN BRODEY: The eruption has been very bizarre, and I have not made a conclusive diagnosis. The eruption has been well controlled with corticosteroids, but I have been reluctant to continue indefinitely. Another biopsy will be performed from the area, as suggested by Dr. Gross. We have a feeling that the diagnosis will prove to be an esoteric one, like extracellular cholesterosis.

A Case for Diagnosis (Polymorphous Light Eruption? Lymphocytoma? Spiegler-Fendt Sarcoid?). Presented by DR. MAURICE J. COSTELLO.

A 44-year-old man, employed as a mechanic, has had a localized eruption of three years' duration, consisting of coin-sized, coalescing, pink, erythematous, infiltrated lesions in the mid-dorsal region of the vertebral column. At present there is a nickel-sized lesion which is undergoing involution as a direct result of roentgen-ray therapy, although similar involution occurred previously when the antimalarial drugs were administered.

Biopsy was suggestive of lymphoblastoma.

Discussion

DR. A. C. CIPOLLARO: I would agree with the diagnosis of lymphocytoma. There are some lymphomas that are difficult to categorize. I think it is relatively benign. I have followed a patient with the chronic form of aleukemic leukemia for 20 years, and he developed several lesions that resembled those seen in the patient presented this evening. The response to irradiation was prompt with comparatively small dosage.

DR. GEORGE M. LEWIS: It is difficult to make a definite diagnosis at this time. The presenter states that it was a firm, dome-shaped lesion and that it regressed under radiotherapy. That is indicative of lymphoblastoma.

DR. ORLANDO CANIZARES: I have had two or three such cases. One woman had a lesion on the face and refused biopsy. I prescribed an antimalarial drug, and the lesion cleared up entirely. I was very pleased with the result until I found she had not taken the drug. This concept of a lymphoblastoma that responds to antimalarials or heals spontaneously is confusing. This type of lesion and other members of the group should be classified separately. I am against calling them lymphoblastomas because the understanding of the medical profession in general is that lymphoblastomas are very malignant lesions.

DR. A. C. CIPOLLARO: The term lymphoblastoma means very little. There are well-known and authenticated cases of leukemia with blood changes that have spontaneously gotten well. Most of these cases, however, do not. There are those that run a chronic course for 10 or 15 years and those that die within two weeks. We have all seen single lesions with blood changes and some with marked alterations. Then there are patients who show cutaneous lesions from head to foot, without blood changes. The hematological manifestations occur long after the cutaneous lesions appear. When we talk about lymphomas we are not talking about a disease with a definite pattern which runs a definite course but about a disease which is extremely variable in appearance and progress.

DR. WILBERT SACHS: Single lesions of so-called lymphoblastomas do not always eventuate into some type of lymphoma. There are single lesions on the sternum which we have had great difficulty in calling lymphoblastoma, and small doses of radiation clear them up. I agree with Dr. Cipollaro that the term does not mean too much.

DR. DAVID BLOOM: Are these lesions which you call lymphobastoma also termed lymphocytoma?

DR. A. C. CIPOLLARO: I think some histologists call them that, but there is a great difference of opinion among pathologists.

DR. PERRY SACHS: You cannot always be sure that it will not be one of the malignant lymphoblastomas. It is difficult to determine at times clinically or microscopically which member of the group is present, and to differentiate it from the benign lesions, such as Spiegler-Fendt sarcoid, lymphadenosis cutis, lymphocytic infiltration, and lymphocytoma. In addition, subacute lupus erythematosis and polymorphous light eruption are also considerations.

DR. A. C. CIPOLLARO: It was Pautrier who originally called attention to these foci of lymphocytes. That was forgotten for some time, and it has become a "new" concept recently. I fully appreciate how difficult it is for a neophyte to keep all of these entities clearly differentiated.

DR. WILBERT SACHS: In the old literature lymphocytoma was synonymous with lymphadenomatosis and Spiegler-Fendt sarcoid.

DR. PAUL GROSS: On the basis of the biopsy findings and the response to x-ray therapy, one should consider the diagnosis of solitary lesion of lymphoblastoma in this case. I believe that the diagnosis of lymphocytoma should be reserved for a specific tumor with germinative centers resembling lymph gland structure.

DR. M. J. COSTELLO: I have frequently seen lesions on the face which were evanescent, with edematous, plaque-like lesions on the malar prominences; they had to be the same disease because, in addition to the identical appearance, they disappeared with the same treatment. Usually the lesions on the back disappear after a time under the same treatment.

DR. PAUL GROSS: If this eruption did completely involute with antimalarial therapy, I must abandon the diagnosis of lymphoblastoma and should accept the diagnosis of lymphocytic infiltration of the skin, in the sense of a polymorphic light eruption.

Nevus Flammeus with Involvement of the Deep Vessels. Presented by DR. JOHN W. DOUGHERTY.

A Negro woman, aged 45, has had a nevus flammeus involving the entire left side of her body since birth. She was first seen, in 1953, in the Outpatient Department of the New York Hospital, with a shallow ulcer 1.5 cm. in diameter on the anterolateral aspect of the lower third of the left leg. She complained of burning pain in the lesion, worse at night. A similar ulcer had developed at the age of 9. Oscillometric studies of the area below the knee showed normal values on the right leg and about one-fourth normal on the left. The ulcer healed in two months with the application of antibiotic ointments. The patient was advised against the use of a pressure dressing by the vascular department.

Roentgenograms of the chest and gastrointestinal tract were normal.

For the past year the patient has had a painful ulcer on the anterior aspect of the left ankle. This is subsiding under local treatment. The ulcer is surrounded by an area of dermatitis, 5 cm. wide.

Discussion

DR. DAVID BLOOM: Unilateral nevi flammei are not infrequently associated with angiomatous lesions in the central nervous system. The Sturge-Weber syndrome in an example of such an association when the nevus flammeus covers one side of the face. It would be of interest to determine whether the circulatory disturbance of the affected extremity in this patient is due to involvement of the central nervous system.

DR. GEORGE M. LEWIS: Will Dr. Dougherty explain the mechanism by which the affected side is cold instead of warm?

DR. MAURICE J. COSTELLO: Many times these patients have hemangiomas of the dorsal vertebrae.

DR. JOHN W. DOUGHERTY: Somebody asked her whether she had back pain, and she said she did not.

DR. PAUL GROSS: I wonder whether the vascular disturbance associated with the nevus could be due to involvement of the vasa nervorum?

DR. WILBERT SACHS: How would you diagnose a thing like that? I do not think anybody could do it, except at autopsy or operation.

DR. PAUL GROSS: Some of the neurovascular manifestations of livedo reticularis with summer

ulcerations have been explained by involvement of the vasa nervorum.

DR. JOHN W. DOUGHERTY: The feeling was that that extremity was colder for two reasons: first, that it is radiating an exceptional amount of heat, and second, that perhaps there is a reflex effect on the deeper vessels so that she is not getting as much blood in that extremity as in the contralateral one. Deep circulation was proved to be impaired on the left side by oscillometric studies. Whether it is purely a structural or a neurogenous element, we do not know.

Basal-Cell Epithelioma Treated by Prolonged Fractional Superficial Roentgen Ray Therapy. Presented by DR. MAURICE J. COSTELLO.

Subcutaneous Nodular Basal-Cell Epithelioma Originating in a Sebaceous Cyst. Presented by DR. MAURICE J. COSTELLO.

Dermatitis Herpetiformis, Polymorphous Pustular Type. Presented by DR. MAURICE J. COSTELLO.

Adenoma Sebaceum Treated by Dermabrasion and Cautery. Presented by DR. MAURICE J. COSTELLO.

Pustular Psoriasis. Presented by DR. THOMAS N. GRAHAM.

A Case for Diagnosis (Polymorphous Light Eruption?). Presented by DR. MAURICE J. COSTELLO.

Erythema Multiforme Symptomaticum (Due to Herpes Simplex? Drug Eruption?). Presented by DR. PAUL GROSS.

Atopic Dermatitis in Three Generations. Presented by DR. DAVID BLOOM.

A Case for Diagnosis (Accessory Mamma? Lipoma?). Presented by DR. DAVID BLOOM.

Familial Benign Chronic Pemphigus (Hailey-Hailey). Presented by DR. NATHAN SOBEL.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Maurice M. Tolman, M.D., President
Paul J. Catinella, M.D., Secretary

Feb. 12, 1958

Oligophrenia, Ichthyosis, and Spastic Diplegia. (?Sjogren-Larsson Syndrome). Presented by DR. CHESTER FRAZIER.

A boy aged 23 months has been followed since the age of 9 months at Children's Hospital because of cerebral palsy and mental retardation. Four weeks ago he was admitted to Massachusetts General Hospital with a clearing eruption of chickenpox and generalized convulsions. In September, 1957, he had had a seizure with acute laryngotracheobronchitis. Until his admission he had had no anticonvulsant therapy. The patient's skin was normal at birth, but he later developed a scaly eruption on the legs, with dry skin elsewhere.

There is an area of pronounced scaling on both legs, giving the appearance of an alligator-like skin. The scales themselves are 1 to 2 cm. in diameter.

The patient is within the normal percentile of growth and development curves. Roentgenograms of the skull and an electroencephalogram were normal. The blood sugar values were normal. Examinations and culture of the spinal fluid revealed no abnormalities.

Discussion

DR. R. NEAL SCHNEIDERMAN (by invitation): This child was first presented to us by Dr. Dodge, of the Pediatric Neurology Department, as a possible case of a new syndrome, described in the *A. M. A. Archives of Neurology and Psychiatry* by two authors, Sjogren and Larsson, as being "oligophrenia in combination with congenital ichthyosis and spastic disorders." Twenty-eight cases had been seen by the authors. Characteristically, the mental deficiency manifests itself as an I. Q. of usually less than 30. In three of the cases it was between 30 and 50. The spastic disorders were usually those of cerebral palsy. All 28 cases had congenital ichthyosiform erythroderma, which varied greatly in degree of involvement but manifested itself usually at birth as erythroderma coincident with or followed by generalized scaling. As the erythroderma faded, scaling usually continued.

From these 28 cases, 2,376 ancestors were traced, and it was found that the syndrome presented itself either as the triad or not at all.

It was felt that the diagnosis could be made clinically because of the extreme rarity of this combination. Almost all the cases were traced back to one of the northeastern counties in Sweden.

The life expectancy in these patients was only 50% of the normal, and genealogic studies showed that the syndrome began 600 years ago with one person who had a mutation of one gene.

We feel that this child probably does not fit into this syndrome, since the ichthyosis is not that of the congenital ichthyosiform erythrodermic type because the flexural areas are not involved. However, it is well known that ichthyosis is not infrequently found to be associated with other ectodermal defects, such as infantilism, dwarfism, genital atrophy, tetany, epilepsy, polyneuritis, mental deficiency, delayed dentition, arachnodactyly, and macular atrophy. We felt this case would be of interest because there is at least a possibility that the child fits into this syndrome.

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Histiocytosis. Presented by Dr. Walter F. Lever.

A boy aged 7 months was born with a "heat rash," which partially cleared until the age of 4 weeks, when it began to increase and became papular. At the same time the patient developed photophobia, and it was noticed that a peculiar tissue was covering part of the iris. Biopsy of this material was performed, and glaucoma was found to be present. In the meantime, from a few papular lesions on the scalp the eruption became more extensive, covering the entire scalp and face as well as the upper part of the trunk. A few of these lesions developed central ulceration. Biopsy of these lesions was performed. The child was found to have an enlarged liver, which was palpable 5 cm. below the costal margin. The spleen could not be felt.

There are numerous waxy, papular lesions arising from apparently normal skin on the scalp, face, and trunk.

Normal findings included blood cell counts, roentgenograms of the skull and long bones, and electrolyte, and bone marrow studies. The cholesterol was 144 mg. %.

Radiotherapy was given in a dosage of 300 r to each eye and to selected skin lesions, with no dramatic response in the latter and no progression of the ocular lesions. Cortisone was started, 100 mg. daily for 18 days, with questionable response. The dosage was reduced to 60 mg. per day and chlorambucil 0.5 mg. per day was started, with some temporary improvement. The patient is now on 10 mg. of cortisone and 2 mg. of chlorambucil, as well as potassium chloride and Diamox.

A baby girl aged 5½ months had been well until she was 7 weeks of age, when she developed lesions on her scalp and one on the back. Several weeks later two of the lesions seemed to undergo central necrosis. The lesions have been getting more numerous, however, during the past few weeks. The child is well otherwise.

There are several waxy, nodular lesions on the scalp, from 1 to 3 mm. in diameter, and one waxy nodule on the back.

The blood cell count, urinalysis, and survey of the bones were normal.

Discussion

Dr. Jacob Swartz: If I had seen the first case clinically I would have called it nevoxanthoendothelioma. I would like Dr. Lever to give us the differential diagnosis of the two diseases, clinically or histologically.

Dr. Francis P. McCarthy: In the first case I understand giant cells were demonstrated but none were present in the second case. The so-called Touton giant cell is usually found in nevoxanthomatous lesions.

Dr. Walter F. Lever: In answer to both Dr. Swartz and Dr. McCarthy, the histologic diagnosis in the first case was nevoxanthoendothelioma, because in the infiltrate, besides histiocytes, there were a fair number of bizarre giant cells. At that time the child had only a few lesions, but now there are hundreds, and the liver is enlarged. On that basis it was felt that the diagnosis should be changed to histiocytosis.

In the second case, the biopsy specimen showed only histiocytes and no giant cells of any type, and so on a histological basis a diagnosis of histiocytosis was made. The clinical picture would fit in more with nevoxanthoendothelioma. That brings into the limelight the relationship between nevoxanthoendothelioma and so-called histiocytosis of the Letterer-Siwe type or the Hand-Schüller-Christian type.

I am interested in Dr. Helwig's statement—he has had a large number of cases of nevoxanthoendothelioma—that there is no reason to assume that it is an abortive type of Hand-Schüller-Christian disease. On the other hand, other authors, such as Thannhauser and Crocker, favor that view and believe that nevoxanthoendothelioma is not a histiocytoma. I would say that the two patients presented today would make me feel that the latter view has more justification than the former, because in the first patient we actually saw the transition take place. I should greatly hesitate to call the first case nevoxanthoendothelioma merely on the clinical evidence now present.

Discoid Lupus Erythematosus with Conjunctivitis and Scarring of Eyelids: Tuberculosis?. Presented by Dr. Maurice M. Tolman.

A Canadian woman, aged 55, has had an eruption of 32 years' duration, with gradual involvement of the entire face. Scarring of nose and eyelids was first noted in 1955.

Most of the face is involved, with areas of atrophy and active, red, scaling lesions. There is ectropion of both lower lids, more pronounced on the left. Scarring is noted especially about the nose.

Urinalysis and blood cell counts were normal. A tuberculin test with purified protein derivative No. 2 was strongly positive.

Chloroquine diphosphate, 0.75 gm. daily, has been given for the past 15 months, with improvement.

Discussion

Dr. Maurice M. Tolman: I presented this case because, although when she was first seen in this clinic we knew that the diagnosis had been proven elsewhere by biopsy and that she had been treated with what is now accepted therapy. I had never seen so much atrophic scarring of the nose to the extent that the cartilage seemed to be involved, and

especially of the eyelid; nor had anyone else I asked. I received no help from the texts, but in the literature I found one reference (*Arch. Dermat. & Syph.* 38:671 [Oct.] 1938, and 42:181 [July] 1940) in the Society Transactions. A case presented before the Bronx Dermatological Society and the New York Academy of Medicine is a prototype of this one, a woman with no lupus erythematosus elsewhere but with involvement of the conjunctiva, leading to scarring and subsequent ectropion. Like this patient, she had a hypersensitivity to tuberculin, with almost a necrotic reaction to the test. During the discussion on that case the question came up as to whether two entities were involved. Could this woman have lupus erythematosus, as demonstrated by the histology and the clinical picture, and also have tuberculosis or possibly lupus vulgaris involving the eyelids and the nose? What is taking place in the eyelids and the marginal conjunctivae—a degenerative change of carcinomatous nature, which frequently occurs in lupus erythematosus? We do not quite have the courage to make a biopsy of the eyelids at this time.

Those who saw the case in New York said that, while they had heard of and occasionally seen lupus erythematosus involving the conjunctiva, it is extremely rare, and they advised treatment for some time. This, of course, was in the prechloroquine days.

The patient is presented for discussion from that point of view. How many of you have seen this type of syndrome, and what can be done about it?

DR. FRANCIS P. MCCARTHY: Was the primary involvement on the eyelid, on the skin, or on the palpebral conjunctiva?

DR. MAURICE M. TOLMAN: On the palpebral conjunctiva.

DR. WALTER F. LEVER: I have seen this more than once but usually just as a single patch on an eyelid, extending to the conjunctiva.

DR. ROBERT F. TILLEY: I would favor immediate biopsy to exclude the possibility of epithelioma.

DR. MAURICE M. TOLMAN: If we perform a biopsy and it turns out to be lupus erythematosus, might we not be contributing to the ectropion? We might try the therapeutic test first.

DR. ROBERT F. TILLEY: There will have to be plastic repair of that eyelid anyway.

DR. ALFRED HOLLANDER: Is the entire conjunctiva palpebralis involved? Since someone has answered that it seems to be, could the ectropion be caused by traction from scar tissue?

DR. NEVILLE KIRSCH: The left lower lid was markedly infiltrated. It had more of a nodular feel (at least it appears to be linear), and I would suspect there may be carcinomatous degeneration.

DR. E. MYLES STANDISH: Apparently the only medication given was a dosage of 0.75 gm. of chloroquine diphosphate. We have been led to believe that chloroquine phosphate (Aralen) might possibly do some damage to the kidneys in the long run. Are you using frequent controls?

DR. MAURICE M. TOLMAN: No.

DR. JAMES PATTERSON (by invitation): She has taken three tablets a day, 750 mg., of chloroquine diphosphate, somewhat intermittently.

A Case for Diagnosis (Nevus Lateris with Neuro-Dermatitis? Discoid Lupus Erythematosus?). Presented by DR. ROBERT F. TILLEY.

Discussion

DR. NEVILLE KIRSCH: I agree with the diagnosis of nevus unius lateris, and I believe any nevus of this sort should be excised. In the *Archives of Surgery* 43:341 (Sept.) 1941, Pack and Sunderland presented an excellent summary of a group of cases in which the incidence of carcinomatous degeneration was significant, and they advised excision of every linear nevus of this type.

DR. HERBERT MESCON: The group at the Memorial Hospital sees those cases that do become malignant—juvenile melanomas, warts, or what have you—and not the others, and so their statistics are loaded. I think the experience of the majority is that this is a relatively benign lesion, and I would question whether the Memoral Hospital series is representative enough to indicate whether or not malignancy is coincidental.

DR. MAURICE M. TOLMAN: It has been my experience that in these cases the incidence of keloids following electrosurgery was high, and so I make it a point, in those who come under my instruction, by all means to avoid it, if possible, and to use surgical excision.

DR. FRANCIS P. MCCARTHY: You do get a higher percentage of keloids, especially in young children, irrespective of modality.

DR. CHARLES SHEARD: I think the cosmetic result in this case, after excision by a skilled plastic surgeon, is not as good as in those done by dermatologists.

A Case for Diagnosis (Atypical Dermatitis Herpetiformis? Chronic Benign Familial Pemphigus?). Presented by DR. NEVILLE KIRSCH.

A draftsman, aged 24, has had a generalized eruption since birth, which is accentuated over the entire trunk. All his life, red, scaling, peeling patches have appeared on the entire cutaneous surface except the palms and soles. There is practically no itching, although at times there are mild burning sensations. He has never been free of the eruption. There is no family history of a similar dermatosis. It appears to be aggravated in summer, even though sweating is present and normal in amount. He has never shown vesiculation or

bullae. There has been no loss of weight, systemic disturbances, or neurologic symptoms.

There is a generalized eruption showing gyrate, arciform, serpiginous, erythematous, scaling lesions and patches. Interspersed with these are discrete and grouped erythematous maculopapular lesions. There is diffuse scaling of the scalp. There is no adenopathy or disturbance of the hair or nails. Redness and some scaling of the margins of the eyelids are present but no cataracts or disturbances in the ocular structures. Some hyperpigmented patches are noted, most prominently on the lower extremities. There are no vesicles, bullae, erosions, or lesions of the mucous membranes.

The hemoglobin was 92%; hematocrit, 49, and white blood cells, 6,600, with polymorphonuclear leukocytes, 52%, lymphocytes, 32%, eosinophils, 7%, and monocytes, 9%. Another blood cell count was normal except for 10% eosinophils. The urine was completely normal. The sedimentation rate was 25 mm. in one hour. A biopsy specimen, taken at the Lahey Clinic, was reported as showing possible Hailey-Hailey disease or dermatitis herpetiformis. Patch tests to 30% potassium iodide and 30% potassium bromide were negative. Scrapings for fungi and culture on Sabouraud's medium were negative.

Biopsy of the skin, read by Dr. Sachs, was as follows: "The composite picture of numerous sections showed superficial vessels to be dilated, and about them was a focal and diffuse reaction, small round and wandering connective tissue cells. In some papillary bodies were polymorphonuclear cells and eosinophils. The epidermis was dry and acanthotic. The palisade margin was intact, and there was a small amount of parakeratosis. None of the sections showed any evidence of chronic benign familial pemphigus. While there was a suspicion of dermatitis herpetiformis, there was no vesicle formation except for a very small one in epidermis." Dr. Sachs concluded that he was inclined to feel the slides probably represented a nummular eczema, although dermatitis herpetiformis was a possibility.

Discussion

DR. NEVILLE KIRSCH: The eruption has never gone into any remissive phase. It has always been just as you saw it today. The patient was originally seen at the Lahey Clinic, where biopsy was suggestive of dermatitis herpetiformis, but he failed to improve on sulfapyridine. When I saw him I gave him Promacetin, which brought no relief, and two courses of arsenotherapy were given, without any remission. The eruption was much worse during the summer, when he was perspiring. No other member of the family has any type of skin disturbance. This man has no itching at all. He is a perfectly placid, calm gentleman, gainfully employed; at no stage of the eruption have there been any vesicles or bullae or any milia. This is the first such case I have seen or even heard about.

DR. FRANCIS P. MCCARTHY: How long after birth did this eruption begin?

DR. MAURICE M. TOLMAN: Three days.

DR. WALTER F. LEVER: I still favor a diagnosis of Hailey-Hailey disease. I think this case resembles the cases of that disease that were originally described by Ayres and Anderson as cases of dermatitis herpetiformis repens. In such a situation one has to take multiple biopsy specimens. The fact that there are no blisters, clinically, does not mean that there are no epithelial detachments, histologically. If the patient would watch for very early lesions and if a biopsy were done, then it might reveal something, whereas those presented today were entirely nonspecific.

DR. JOHN FROMER: We also entertained the diagnosis of Hailey-Hailey disease because at times when I saw this patient, some 10 years ago and for at least 2 or 3 years thereafter, he would come in, as a youngster, with his undershirt full of crusts and serous discharge. He actually smelled like a patient with active pemphigus.

DR. MAURAY J. TYE: This case recalls to mind a patient I saw several years ago with generalized bullous Darier's disease. In view of the history of exacerbations following exposure to ultraviolet rays, might I suggest that a small area be exposed and a biopsy performed? It might be that then a bulla or vesicle would be found intact.

DR. ALFRED HOLLANDER: Hailey-Hailey's disease is not as widespread as this. Is it not characteristic of that disease that the lesions are more localized?

DR. WALTER F. LEVER: The average case is localized to a few areas, but several very extensive cases have been reported in the literature. One was recently reported, in Germany, by Herzberg (*Arch. klin. u. exper. Dermat.* 202:21, 1955).

DR. NEVILLE KIRSCH: I gave the patient some Meticorten for a while, and he became much worse, and so I discontinued it immediately.

Lupus Erythematosus Profundus: Discoid Lupus Erythematosus of the Scalp. Presented by DR. MAURICE M. TOLMAN.

Neurilemmoma. Presented by DR. A. A. SOIFER.

Chronic Folliculitis and Furunculosis. Presented by DR. PAUL J. CATINELLA.

A Case for Diagnosis (Psoriasis?). Presented by DR. HERBERT MESCON.

Acrokeratosis Verruciformis (Hopf). ?Early Mild Scleroderma. Presented by DR. WALTER F. LEVER.

Scrofuloderma Secondary to Tuberculosis of Parasternal Lymph Nodes. Presented by DR. PHILIP MCCARTHY.

A Case for Diagnosis (Dermatitis Nodularis Necrotica? Papulonecrotic Tuberculid?). Presented by DR. JOHN ADAMS JR.

Mycosis Fungoides and Chronic Lymphatic Leukemia. Presented by Dr. John Adams Jr.

Ehlers-Danlos Syndrome. Presented by Dr. William R. Hill.

Granuloma Annulare. Presented by Dr. Robert F. Tilley.

Congenital Alopecia. Presented by Dr. Paul J. Catinella.

Granuloma Annulare. Presented by Dr. Paul J. Catinella.

Schamberg's Disease. Presented by Dr. Philip McCarthy.

Pili Torti. Presented by Dr. Joseph Goodman.

A Case for Diagnosis (Drug Eruption? Erythema Multiforme?). Presented by Dr. Herbert Mescon.

NEW YORK DERMATOLOGICAL SOCIETY

J. Lowry Miller, M.D., President

Maurice J. Costello, M.D., Secretary

Feb. 25, 1958

Letterer-Siwe Disease. Presented by Dr. Orlando Canizares.

A 17-month-old baby boy was referred to me by his pediatrician on Jan. 15, 1957, because of a perianal ulceration of six weeks' duration. There was an erosive lesion extending about 2 cm. around the anus. The lesion was rather superficial and showed evidence of secondary infection. There was also some crusting of the scalp. Since the patient had spent several months in Brazil, examinations for amebae and leishmaniae were carried out, with negative results. The lesion improved with antibiotic therapy, but it did not heal.

The child was seen again on July 26, presenting a peculiar eruption on the scalp, face, axillae, and groins. The lesions were scaly and crusted papules, 2 to 3 mm. in diameter, on apparently normal or slightly erythematous skin. A diagnosis of Letterer-Siwe disease was made clinically and confirmed by biopsy.

Prednisone, 5 mg. daily, was prescribed, and grenz rays, 200 r, were administered in four successive weeks. The cutaneous lesions improved considerably, but the anal ulceration failed to improve. The mother consulted several physicians, and the child was hospitalized in two institutions. During the second hospitalization the cervical and submental glands enarged and splenomegaly and hepatomegaly developed. The patient received deep x-ray therapy to both sides of the abdomen, 50 r daily for three weeks, with little diminution of the hepatomegaly and splenomegaly but clearing of the cutaneous lesions over the irradiated area.

At present there is a vesiculopustular eruption on both sides of the neck and the scalp, axillae, and groins. There are also many crusted papules. Both sides of the abdomen, where the deep x-ray therapy was administered, show almost complete healing of lesions. There is pronounced cervical and submental adenopathy.

Roentgenograms of the long bones were normal. Roentgenograms of the scalp showed some defect, but not characteristic of this disease. During hospitalization the patient had a low grade anemia, for which he received several blood transfusions.*

Discussion

Dr. M. J. Costello: I had this baby under my care at Lenox Hill Hospital for several weeks. We made a diagnosis of reticuloendotheliosis. On the scalp the eruption looks like seborrheic dermatitis; on the margins, like impetigo, and on the body it is similar to lichen planus. Dr. Dougherty presented a sister and brother with this condition last year; it had been present for some time.

Dr. Carl T. Nelson: This is an example of histiocytosis X, or nonlipid reticuloendotheliosis. The eruption, including that on the scalp and palms, is quite typical. The prognosis is completely gloomy. In the cases that have been treated with radiation, large doses of steroids, etc., at Babies Hospital, there has been no appreciable prolongation of life.

Dr. Orlando Canizares: This has been a problem primarily, of course, from the standpoint of prognosis but also from that of poor cooperation of the parents, especially the mother. She has been frightened, keeps going to different hospitals, and gives no one a chance to treat the child. Finally, at Bronx Hospital, they gave what they considered to be the maximum amount of deep x-ray therapy. I shall continue to use Meticorten unless there are other suggestions.

Junction Nevus. Presented by Dr. George M. Lewis.

A Puerto Rican boy, aged 2½ years, has had a brown, asymptomatic mole on the right thigh since birth. When he was first seen at the New York Hospital Dermatology Clinic, in December, 1956, the lesion measured 3 by 3 cm.

There is a well-marginated, brown, slightly raised, hairy lesion on the lateral aspect of the right thigh above the knee. The increase, to 3.5 by 3.5 cm., in size during the past year is considered to be due to natural growth.

Biopsy was reported as junction nevus (inactive).

Submitted for publication July 19, 1958.

* The patient died on April 15, 1958.

Discussion

DR. M. J. COSTELLO: I imagine the case is presented for suggestions as to therapy. It looked like a pigmented, hairy mole, and since it is not a cosmetic deformity I would be inclined to leave it alone. The only reason for removal would be the parents' insistence on it, for cosmetic reasons.

DR. LESLIE P. BARKER: I would not treat this lesion.

DR. CARL T. NELSON: This is a light brown, hairy nevus, and I, too, would leave it alone.

DR. GEORGE C. ANDREWS: I would leave it alone, but when the child gets older and goes to school I would consider excision and graft. I know of a case where the patient wanted to get rid of the lesion because it was unsightly in a bathing suit. At this age the mortality from general anesthesia is too great.

DR. GERALD F. MACHACEK: I disagree with those who would leave it alone. In the few cases I have observed over a long period the lesion became very large, and it became difficult to do a nice cosmetic excision. I agree with Dr. Andrews that it should be excised at an appropriate time.

DR. A. C. CIPOLLARO: Evidently those who believe in leaving this lesion alone think that is safe and that it is benign. Those who would excise it think that would be a safe procedure. Before we were made aware of the possible danger of junction nevi we did not do biopsies and many of these lesions were treated with solid carbon dioxide or electrosurgery. From the thousands of lesions so treated, statistics fail to show any significant incidence of melanoma. Many junctional nevi were treated as ordinary pigmented and hairy moles, with cautery, electrosurgery, galvanic current, or solid carbon dioxide, without any serious complications. The tendency today, however, is to excise and examine histologically all lesions suspected of being junctional nevi.

DR. FRANK C. CORMIA: This is a benign lesion, and I doubt that it will ever show malignancy. I agree with Dr. Andrews. I think as the child grows older he may want to have something done. At present, I would leave it alone. At New York Hospital we have done repeated partial excisions. I would be against electrocoagulation because of the resultant scar.

DR. A. N. DOMONKOS (by invitation): It is interesting to note that young children usually have a junction type of nevus, and later on it is said they are epidermal. I wonder whether all hairy nevi in children are of junctional type. It would be very interesting, if the lesion were not removed, to do a biopsy and see if this phenomenon appears. I would hesitate to excise a junction nevus in steps, mainly because of the traumatic influence. If it is to be removed, it would be better to excise it at one time and graft it.

DR. DOUGLAS TORRE (by invitation): I agree with Dr. Cormia. I had an opportunity to examine the patient at the clinic and think that the lesion could be easily removed by serial excision. If it is done before puberty there would not seem to be any danger.

DR. WILBERT SACHS: Clinically, I would not think of anything but intraepidermal nevus. Microscopically, however, there are nests in the epidermis, and I thought it was more or less inflammatory. Under better circumstances I could perhaps arrive at a better diagnosis. Looking at the slide, there is no question that it is a nevus and that these nests must be of the junction type. I can not go along with the statement that a junction nevus later on in life becomes benign.

DR. GEORGE M. LEWIS: The brown, hairy nevus has had the reputation of being essentially benign. While instances of malignant degeneration have been reported, this danger is currently often overdrawn. It is certainly impractical to excise every junction nevus, and it is my feeling that good judgment in selecting suitable cases for prophylactic therapy is important.

A Case for Diagnosis (Rosacea-like Tuberculid?). Presented by DR. ORLANDO CANIZARES.

A white woman, aged 38, consulted me on Sept. 12, 1957, because of an eruption on the face of over two years' duration. Her mother has diabetes. There is no history of tuberculosis in the family.

The patient has had the usual childhood diseases but no serious illnesses. A complete physical examination, including x-ray examination of the chest, was "normal."

About three years ago, after her return from a trip to South America, where she was much exposed to sunlight, the patient noted some small lesions on both sides of the chin. The lesions are rather dry and leave depressed scars on healing. Several months after the onset of the facial lesions the patient noticed a few elevated brownish lesions on the forearms. These have not changed. The patient consulted a dermatologist, who made a diagnosis of rosacea and administered seven x-ray treatments. Later, carbon dioxide slush was applied. The lesions failed to improve.

The patient also has dermatophytosis of the feet, with onychomycosis. There has been no loss of weight or impairment of the general health.

There is an eruption on both sides of the chin, consisting of two patches, oval and approximately 4 cm. in the long diameter, where most of the lesions are located. The individual lesions are slightly elevated, yellowish-brown papules, varying from 2 to 4 mm. in diameter. There are also depressed scars of about the same size. The rest of the face is clear. The lesions under diascopic examination have a yellowish color. On the extensor aspect of the forearms, near the elbows, there are

a few elevated, round lesions with a flat surface, 6 to 8 mm. in diameter. They are reddish yellow and asymptomatic. Lesions of dermatophytosis and onychomycosis are seen on the feet.

From Sept. 12 to Oct. 21 the patient received tetracycline (Achromycin), 250 mg. daily, and salicylic acid was applied. There was no appreciable improvement. From Oct. 21 to the present she has received isonicotinic acid hydrazide (Rimifon), 50 mg. in increasing doses up to 200 mg. daily. Cold quartz light has been applied locally. There has been definite improvement.

Biopsy of a somewhat distorted specimen showed an attenuated epidermis covered by a thick, parakeratotic stratum corneum. The entire cutis in these sections had been replaced by a granuloma, which consisted of epithelioid cells and numerous lymphocytes. It was also somewhat hemorrhagic, evidently due to trauma. It was thought that the lesion was probably a tuberculid and possibly sarcoid. Diagnosis: cutaneous granuloma, rosacea-like tuberculid.

A tuberculin test was performed on Feb. 24 with 0.0001 mg. of purified protein derivative (first-strength solution).

Discussion

DR. CARL T. NELSON: I have little to say except to raise the possibility of a papular type of sarcoid.

DR. GERALD F. MACHACEK: I would favor the diagnosis of micropapular sarcoid rather than tuberculid.

DR. HENRY E. MICHELSON (by invitation): I do not believe rosacea-like tuberculid of the Lewandowsky type exists at all, and I believe that is now international opinion. You will see fewer and fewer diagnoses of Lewandowsky's tuberculid and more and more of lupoid rosacea. I have come to the conclusion that nodular lesions, negative on diascopy, are lupoid rosacea. This girl was hypertrichotic, and that helps a good deal. If you make a diagnosis of tuberculid you are making a diagnosis of tuberculosis. I think all cases are types of rosacea, in a sliding scale.

DR. GERALD F. MACHACEK: You mean lupoid rosacea is rosacea with a lupoid appearance?

DR. HENRY E. MICHELSON: Yes.

DR. A. C. CIPOLLARO: I have been interested for many years in tuberculosis of the skin. During the last 30 years there have been great changes in the evolution of diseases. Tuberculosis of other parts of the body was a great deal more prevalent than it is today. We don't see lupus vulgaris or rosacea-like tuberculid and not even reactions to tuberculin, as we did 30 years ago. Clinically, I do not consider this to be a case of rosacea-like tuberculid of Lewandowsky because there is no rosacea element. With a histology that suggests sarcoid and with the lesions on the arm, I would consider the papular type of sarcoidosis, rather than rosacea-like tuberculid, or lupoid sycosis. The fact that the patient did not have a pronounced reaction to tuberculin fits in better with sarcoid than with rosacea-like tuberculid of Lewandowsky.

DR. GEORGE C. ANDREWS: The lesions on the arms would fit in with sarcoidosis.

DR. FRANK E. CORMIA: I, too, did not see any rosacea. I agree with Dr. Michelson that there is no such entity as rosacea-like tuberculid of Lewandowsky. I thought of the possibility of micropapular tuberculid but believe that it might be sarcoidosis. The lesions on the arm are suggestive of sarcoid; this possibility should be investigated.

DR. MAURICE J. COSTELLO: I would be inclined to agree with sarcoid, and the lesions on the arms suggest it. Because of the character and size of the lesions I think the pathology does not militate against that diagnosis.

DR. L. P. BARKER: Because of the appearance of the lesions on the arms and the absence of rosacea of the face I would favor a diagnosis of papular sarcoid.

DR. ORLANDO CANIZARES: This patient was presented for diagnosis. She has been reluctant to have a biopsy, and so, when she said I could take one, I chose the face. I am going to talk her into having one from the arm, which I think would be helpful.

Reticulum-Cell Sarcoma. Presented by DR. CARL T. NELSON.

A white woman, aged 50, is presented from Presbyterian Hospital, with lesions of the left leg of nine months' duration. The patient first noted a crusted ulcer in the left anterior tibial area; this healed slowly but was succeeded by several violaceous nodules in the surrounding skin. Some of these involuted spontaneously, leaving residual pigmentation; others formed crusted ulcerations which healed with difficulty. There was no definite history of trauma or insect bites. Treatment for stasic ulcers by another physician yielded no benefit.

At present the patient shows two violaceous, proliferative, healed nodules in the left anterior tibial area. These are 1.5 to 2.0 cm. in diameter. There is some surrounding dusky erythema. On the lateral surface of the leg there are healed, pigmented lesions. Physical examination is otherwise not remarkable.

A complete blood cell count and urinalysis were within normal limits.

Biopsy of a granulomatous ulcer showed a sclerotic cutis infiltrated with large cells with hyperchromatic nuclei. The infiltration suggested a diagnosis of reticulum-cell sarcoma. There was also a striking infiltration of polymorphonuclear leukocytes.

There has been no treatment, but irradiation is contemplated.

Discussion

DR. L. P. BARKER: I could not make a clinical diagnosis of reticulum-cell sarcoma on the lesion that is present today. It looks more like a subsiding inflammatory lesion, perhaps a drug eruption. I suppose, however, one cannot discount the pathology of the original lesion.

DR. GEORGE C. ANDREWS: I feel as Dr. Barker does, that there is not enough clinical evidence to make a diagnosis. It is certainly very unusual for a reticulum-cell sarcoma to disappear spontaneously, and so we may be dealing with some other type of lymphoblastoma. For the time being, it seems to me we could keep the patient under observation.

DR. GERALD F. MACHACEK: There is a great deal of difference between seeing a case clinically and seeing merely a miniscule portion of skin. I would say there is a possibility of insect bite, particularly in view of the fact that the lesion has disappeared. I showed the slide to very able pathologists, and they all said it was not insect bite but reticulum-cell sarcoma. I would still say the biopsy was that of reticulum-cell sarcoma. I have seen sarcoma begin in just this way, though I can not say the lesion disappeared completely. I looked at the biopsy specimen again yesterday, and not knowing the case, I would say it was lymphosarcoma. Now that I see the woman, I would say insect bite.

DR. A. C. CIPOLLARO: The diagnosis of reticulum-cell sarcoma is one that has been made in comparatively recent years; it is not clearly defined or differentiated from the other lymphomas, particularly mycosis fungoides. At times it is seen in the terminal stages of mycosis fungoides. At other times the histologist reports reticulum-cell sarcoma in lesions removed from patients with classical clinical mycosis fungoides. From the cases I have observed, I gather the impression that reticulum-cell sarcoma is another of the multiple variants of mycosis fungoides, and so the prognosis is no worse than that of the latter. The lymphomas run an unpredictable course. Some localized lesions of lymphoblastoma are sometimes associated with blood changes—more often they are not. They run, of course, over many years and respond readily to small amounts of radiation. I have an optimistic attitude toward these cases, and I would certainly treat this patient with x-rays.

DR. FRANK E. CORMIA: I should like to ask the presenter whether the fact that some of these lesions are involuting spontaneously might alter the diagnosis. The cases of reticulum-cell sarcoma I recall have been progressive. I do not remember seeing patients with spontaneous remissions.

DR. A. N. DOMONKOS (by invitation): Since there has been such nice involution from deep nodules to almost flat, pale lesions in the skin, I would withhold x-ray therapy at present. The most important thing about this group of lesions is that one should not attempt to give a large amount of x-rays because the lesions do involute nicely on small doses.

DR. DOUGLAS TORRE (by invitation): As to the use of x-rays, I should first perform another biopsy, since the first one seemed to be somewhat obscured by inflammatory cells. If there were no sarcoma cells present I would not give x-ray therapy.

DR. CARL T. NELSON: I think Dr. Cormia's point about the clinical involution of the lesion raises a serious question regarding the accuracy of the diagnosis. Nevertheless, one cannot disregard the microscopic picture. Dr. Torre's point that another biopsy is indicated is well taken. If the microscopic findings are substantiated, then I believe x-ray therapy will be indicated.

Idiopathic Atrophoderma of Pasini and Pierini.

Presented by DR. ORLANDO CANIZARES.

A 23-year-old Puerto Rican woman reported to the outpatient clinic of Bellevue Hospital because of an extensive hyperpigmented eruption involving the trunk and upper extremities, of 10 years' duration. She stated that the eruption developed rather suddenly on the chest and trunk without any previous subjective symptoms and that its characteristics have remained the same. The lesions have never been indurated to the touch. In recent years some new lesions have gradually appeared. First they present a brownish discoloration, and later they become somewhat depressed. There is no history of ingestion of medication.

The patient presents an extensive eruption involving the anterior and posterior aspect of the trunk, sparing the chest, and involving also the flexural aspect of the forearms, the dorsal surface of the proximal and distal interphalangeal joints, and the periungual areas of all fingers and toes. The color varies from light tan to dark brown. On the back the lesions cover wide areas and are definitely depressed. In some there is a "cliff drop" and in others a gradual slant. The surface of the patches, besides their color, is of normal appearance and consistency. There is no edema, induration, elevation, or scaling and no abnormality of sensation. The deeper blood vessels are faintly visible beneath some of the lesions on the forearm.

The blood cell count showed red blood cells 4,100,000, hemoglobin 12 gm., white blood cells 7,750, with neutrophils 56%, lymphocytes 36%, monocytes 2%, and eosinophils 6%. The sedimentation rate was 15 mm. in one hour (Westergren). Total serum proteins were 7.4 mg., with albumin, 4.2 mg. and globulin, 3.2 mg. per 100 cc. Serum protein electrophoretic studies showed 3+ trailing between γ- and β-globulins. The pattern was otherwise normal. The protein-bound iodine was 6.2%. The serum cholesterol was 255; esters, 185 (73%).

The fasting blood sugar was 64 mg. per 100 cc. Serologic tests for syphilis were negative, and urine was normal.

Biopsy: The epidermis was within the range of normal thickness and contour for the site and sex. It was slightly and finely wavy and deeply pigmented with melanin granules in the basal layer. In the upper corium were patent and constricted small blood vessels surrounded by a very few histiocytes and lymphocytes, an occasional mast cell, and melanophages. There was no inflammatory reaction. The collagen fibrils did not appear abnormal, nor were they more or less dense than the normal range. Elastic fibrils were present and also appeared to be within the range of normal. Sweat glands, pilosebaceous follicles, and erector pili muscles were present, and villous hair was seen in the follicles. Fat lobules indented the collagen on the lower border and rose around the hair papillae. A silver stain demonstrated the presence of melanin profusely throughout the epidermis. No amyloid or mucin was present. Diagnosis: hyperpigmented skin.

Discussion

Dr. George C. Andrews: This case belongs in the syndrome described by Pasini and brought to our attention recently by Dr. Canizares, Dr. Torre, and others. It certainly has no clinical resemblance to scleroderma, and there is no history of drug intake to account for the eruption. There is a certain amount of atrophy, which one would not expect from drugs anyway. I agree with the diagnosis as presented.

Dr. Gerald F. Machacek: It is a most remarkable entity. You would think it was a widespread fixed eruption if you looked at it cursorily.

Dr. George M. Lewis: Would Dr. Canizares comment on the incidence of this disease in Europeans and Americans who are native-born?

Dr. A. C. Cipollaro: I am indebted to Dr. Canizares for the knowledge I acquired about this disease. He lent me Pasini's original article and some of Pierini's articles. For several years the disease was forgotten. Pierini's cases came from South America, and Dr. Canizares has reported cases from the United States. I have seen only those he has presented. It is a very interesting disease of obscure etiology and pathogenesis. It is a very peculiar atrophy, unlike any other atrophies we know. Often it resembles scleroderma, and yet the case presented tonight has none of the features of scleroderma.

Dr. George C. Andrews: The first case shown by me was 20 years ago, and all discussed whether or not it was scleroderma, ultimately agreeing that it would evolve into scleroderma with a hidebound condition.

Dr. Frank E. Cormia: Dr. Lewis brought up an interesting question: Is this condition entirely or mainly found in people from Central or South America? I recall examining people from that part of the world and their skins were of a curious soft texture; there seemed to be a lack of resilience. In cases of native-born Americans the atrophy often follows morphea. This seems to be different. There is a curious distribution, and there is no preceding dermatosis. Perhaps Dr. Canizares can enlighten us.

Dr. A. N. Domonkos (by invitation): The case Dr. Andrews presented was an American woman, native-born but of Italian parentage.

Dr. Douglas Torre (by invitation): One of the striking things is the pigmentation. The slight indentation would be hard to pick up in a purely white person, and that might be why Italians and South Americans have reported these cases.

Dr. Maurice J. Costello: I showed a case in 1948, a young married woman with pneumothorax, who had a lesion which covered the whole back. The color was slightly darker than the surrounding skin, and the lesion was slightly depressed. I understand that biopsy specimens of these cases show very little, and no one has seen a case from its inception and followed it through the years. I was under the impression, and everybody agreed, that it was a large plaque of morphea. I am under the impression that this may be just a large localized plaque of morphea. Heretofore we have dealt mostly with Anglo-Saxons, but now we are dealing more with Puerto Ricans and Italians, with darker skins.

Dr. Orlando Canizares: One of the patients I have reported was a blonde and the others have been brunets. The disease was originally described in Italians, and it has also been observed in Argentina. I saw one patient from Morocco. I suppose the higher the normal amount of pigmentation, the more likely the changes are to be noticed. Also the greater the amount of pigment in the skin, the darker the lesions tend to be. When the skin is paler there is a bluish color, because one is seeing the deeper blood vessels through an atrophy as if looking through a smoky glass. As far as the etiology is concerned, Pasini thought it to be related to tuberculosis. His patient had active tuberculosis, and the lesions appeared somewhat later. Pierini was also in favor of that concept, but there is no definite evidence, as in many cases the past history is essentially negative. As for the course of the disease, the lesions just seem to go to a certain level and stay there. The pathologists are discouraged because the histologic changes are minimal. There are some changes in the elastic tissue, as shown by Dr. Perry Sachs.

Psoriatic Erythroderma. Presented by Dr. J. Lowry Miller.

A Negro man, aged 41, has a well-documented history of psoriasis for the past 30 years. In

October, 1957, he noted the onset of an illness characterized by intermittent, severe, shaking chills, anorexia, a weight loss of 30 lb., and the gradual spread of psoriatic lesions to the final evolution of psoriatic erythroderma. Showers of minute pustules, predominant on the palms and soles but present over the entire integument, were a striking feature of the process. He was admitted to Presbyterian Hospital in December. An extensive bacteriological and radiological evaluation failed to demonstrate a cause for the daily rise in temperature up to 102 F. Biopsy of a lymph node and bone marrow did not suggest a lymphomatous process. Local therapy consisted of hydrophilic ointment and potassium permanganate baths.

The hospital course was complicated by an episode of staphylococcal septicemia, which responded to novobiocin. The fever continued, and a blood culture again showed staphylococci. Chloramphenicol was given. Fever continued for several weeks, although the blood cultures became negative. Meticorten, 60 mg. daily, and repository corticotropin injection (ACTH Gel), 40 units daily, were instituted during the eighth week of hospitalization but had no effect on the eruption. Steroids and antibiotics were gradually discontinued during the 10th week, with gradual improvement in the skin. The patient is now receiving local hydrophilic ointment only.

Discussion

Dr. George M. Lewis: In similar cases of erythroderma I have had moderate-to-good success with a program which includes vitamin A, 100,000 to 200,000 units orally a day, antihistaminics in moderate dosage, and a bland local vegetable fat, such as Spry or Crisco. The vegetable grease routine excludes the possibility of a vaselinoderma. The great threat is infection, and if possible the patient should not be hospitalized where the risk of acquiring a staphylococcic infection is great.

Dr. A. C. Cipollaro: The interesting thing to me is the fact that this patient had septicemia. It is difficult to decide whether the pustules on his skin represented septic foci secondary to a staphylococcemia or whether the septicemia followed a primary multiple staphylococcic cutaneous infection. I am inclined to believe that the original source of the septicemia was the pustules on the skin. In some cases of severe psoriasis in patients whose resistance is lowered, extensive secondary pustulation is seen. Pediatricians throughout the country are very much concerned about the increased incidence of staphylococcic infections in some of our hospitals.

Dr. M. J. Costello: Dr. Cipollaro and I had a patient, hospitalized at St. Clare's, with psoriatic erythroderma, and with every rise in temperature there were sheet-like showers of pustules. We gave him all the therapy we thought he could handle, including antibiotics and steroids. The psoriasis improved. He went to Scotland and developed a relapse there, and at autopsy miliary abscesses were found in the kidneys, which may have been the original focus of his disease. I think the prognosis in the patient presented tonight is poor. Only three times have I seen a case such as this.

Dr. Frank E. Cormia: We know that the kidneys may be involved secondarily.

Dr. Carl T. Nelson: This man was a known psoriatic for a number of years, and for some weeks preceding hospitalization he had been febrile. For this reason he was admitted. Dr. Cipollaro's point about the attitude of pediatricians regarding the admission of patients of this type to the hospitals is important. Physicians in charge of adult wards are also very much aware of the same problem. It is now not unusual to admit patients with open skin lesions and have them develop boils and other types of staphylococcic infection. I think we must suspect that the psoriasis was the portal of entry for the Staphylococcus and the resultant bacteremia in this case. It was only after the patient's temperature had become normal and the blood cultures had become sterile that we tried corticosteroid therapy. In retrospect, perhaps the patient would have done better under Dr. Miller's form of treatment.

Dr. George C. Andrews: I believe some internal factor is contributing to the pustulation of the skin and the fever. I do not believe it is just the skin condition that caused the fever. It would be safe to try a hydrophilic dressing on one lesion and see if pustules reappear, to see whether it is just a matter of greasiness or dryness. The pustules might have nothing to do with the psoriasis but come from some other causative factor or might be large Munro abscesses.

Dr. M. J. Costello: The pustles were extremely superficial, without any papular element but just vesicles filled with pus.

Dr. George C. Andrews: Do you think all that trouble could have been caused by steroids?

Dr. J. Lowry Miller: In this case I doubt that they were responsible for the entire condition. Another case comes to mind, a woman who came to me for at least 15 years for psoriasis. She had it on the vulva and always objected very much because of the location. While I was away she went to another doctor for arthritis; he immediately put her on steroids, and the psoriasis completely cleared. Within a year's time exactly the same thing happened as in this patient; she developed generalized erythroderma and died of various and sundry infections, including the kidneys. She was not over 50 when she died, so I have always thought it was a steroid death.

In closing, there is one factor to remember: This man's illness began with chills and fever at

home, with a loss of weight of 30 lb., and so I don't think the cortisone can be blamed for any of the factors present at the onset. On his entering the hospital the blood cultures were negative, then positive, later negative, and again positive; then another antibiotic was given, and he was then put on steroids. In answer to Dr. Costello, the skin was peppered superficially with pinhead-sized vesicles filled with pus. We tried leaving off all greasy ointments, and he became perfectly clear of all pustules. Whether that was fortuitous or not I do not know, because the temperature had begun to fall. We were able to take him off steroids. His whole mental attitude improved concomitantly. I agree with Dr. Cormia. I think the skin can be the source of staphylococcic infection which in turn affects the kidneys. I have a little better prognosis for this man because I think perhaps, by good fortune, he has not developed the multiple abscesses in his kidneys. I should think those were secondary.

Granuloma Annulare, Generalized Unusual Type. Presented by DR. MAURICE J. COSTELLO.

Psoriasis with Koebner Phenomenon. Presented by DR. FRANK E. CORMIA.

Squamous-Cell Epithelioma. Presented by DR. ORLANDO CANIZARES.

Abstracts from Current Literature

Effects on the Skin of Nickel and Chromium Salts. M. H. Samitz and H. Pomerantz, A. M. A. Arch. Indust. Health 18:473 (Dec.) 1958.

Patch-test reactions on persons allergic to nickel sulfate and potassium dichromate were heightened by the addition of sodium lauryl sulfate. Cysteine, glutathione, and ascorbic acid showed a capacity to inactivate patch-test reactions in chromate-sensitive persons, while sodium diethyldithiocarbamate inhibited reactions in nickel-sensitive patients.

Lazar, Chicago.

Corneal Epithelial Changes Occurring During Chloroquine (Aralen) Therapy. L. L. Calkins, A. M. A. Arch. Ophth. 60:981 (Dec.) 1958.

Corneal changes, similar to those seen with quinacrine (Atabrine) therapy, may occur with chloroquine (Aralen) therapy. The principal complaint was fuzziness about objects observed in bright light and halos about lights at night. Improvement or freedom from symptoms resulted from discontinuing the drug. The corneal changes which resemble a rare dystrophic change, cleared with the symptoms.

Lazar, Chicago.

Dermal Vascular Allergides. B. Duperrat and J. Monfort, Ann. dermat. et syph. 85:385-411 (July-Aug.) 1958.

This lengthy article deserves reading in the original. The authors point out that there is a large group of lesions which appear in sensitized subjects; some of these have been known for a century, such as erythema induratum of Bazin, others for a long time, such as erythema nodosum, and yet others are of more recent date. They all have this in common: that certain nodular elements may appear, then disappear rather rapidly, without necessarily ulcerating; that all the elements center about a diseased vessel; that necrosis is common, and that granulomatous changes are secondary. Having said this, one may align these disorders into an uninterrupted series of lesions, ranging from the most benign to the most grave. The allergic nature of the lesions is evident in the nodular allergide of Gougerot and in certain numbers of nodular vascularitides, very probable in periarteritis nodosa and probable in a great number of erythema nodosum and migratory thrombophlebitis. This concept is important because it permits one to orient future therapy, still uncertain, against these morbid states which, curiously enough, continue to increase in daily practice.

Derbes, New Orleans.

Studies on Sterilization of Pathogenic Fungi by Ultraviolet Light. J. Coudert and J. Rondelet, Ann. dermat. et syph. 85:412-419 (July-Aug.) 1958.

The sterilization of barbers' instruments, rendered obligatory in theory by an edict of the Minister of Public Health, is impossible with ultraviolet apparatus currently available.

Derbes, New Orleans.

The Clinical and Diagnostic Importance of Occult Mycotic Foci. T. Schulz, E. Weiss, and M. Oros, Ann. dermat. et syph. 85:420-424 (July-Aug.) 1958.

Many eruptions, considered as dyshidrotic eczema, chronic urticaria, and miliary impetigo, are in reality mycides, susceptible of rapid simple and definitive treatment if one searches out mycotic foci in the interdigital spaces and soles, the submammary regions, and especially the genital and perigenital areas.

Derbes, New Orleans.

Linea Fusca (The Brown Forehead Ring of Andersen, Wernoe and Haxthausen). P. J. Michel, Ann. dermat. et syph. 85:509-521 (Sept.-Oct.) 1958.

The linea fusca was observed by the Danish dermatologists in persons suffering from various affections of the central nervous system (above all in postencephalitic Parkinsonism, nervous system syphilis, tumors, syringomylia, etc.). The author reports 13 personal cases. He believes the condition is in no way rare, is commonest in women, and appears in the most

varied etiologic circumstances. He is inclined to consider it of endocrinosympathetic origin and due to hormonal imbalance.

DERBES, New Orleans.

GENEOLOGY OF A FAMILY OF SUBJECTS AFFECTED WITH SYNDACTYLISM IN FIVE GENERATIONS. M. LEFRANC, Ann. dermat. et syph. 85:527-529 (Oct.) 1958.

This is the family tree of 32 persons, of whom 16 showed the anomaly, 11 were exempt, and 5 were infants who died at an early age. Transmission was by dominant autosomal inheritance.

DERBES, New Orleans.

HISTAMINE IN NORMAL AND PATHOLOGIC SKIN. L. CRAPS and T. INDERBITZIN, Arch. belges dermat. et syph. 13:113-139 (June) 1957.

The authors point out certain technical difficulties but believe that valid results can be obtained in comparing histamine contents in fragments of normal and pathologic skins having exactly identical areas and taken from two symmetrical or closely adjacent points. Average histamine content in skin of trunk and limbs is 8.5μg. per gram, but there are regional and individual variations. In pathologic skin the histamine content is related to the quality of the cellular infiltrate.

DERBES, New Orleans.

RIBONUCLEIC ACID AND PROTEIN SYNTHESIS IN THE EMBRYONIC DEVELOPMENT OF HUMAN SKIN. G. ACHTEN, Arch belges dermat. et syph. 13:140-143 (June) 1957.

Ribonucleic acid and tonofibrils appear at the same time. The ribonucleic acid plays a part in protein synthesis during keratinization, a process accompanied by decreased cellular glycogen content. The infrasebaceous portion of the hair follicle has a passive role in development, hence contains little ribonucleic acid and much glycogen.

DERBES, New Orleans.

GENERALIZED SCLERODERMA, AUTOPSY, SCLERODERMA AND RENAL LESIONS. L. VAN DER MEIREN, G. CARPENT, and P. TOUSSAINT, Arch. belges dermat. et syph. 13:144-148 (June) 1957.

Scleroderma may present signs of severe renal decompensation with uremia, hypertension, hypertensive retinopathy, hematuria, and albuminuria. It has a very acute evolution and ends fatally. Renal lesions show a profound involvement of the renal parenchyme: interlobular infarcts and fibrinoid necrosis of the afferent arteries. These lesions are identical to those of malignant nephroangiosclerosis contemporary with malignant hypertension.

DERBES, New Orleans.

HERPES GESTATIONIS: ANATOMOPATHOLOGIC STUDY OF FETAL LESIONS. P. TOUSSAINT and R. SCHOYSMAN, Arch. belges dermat. et syph. 13:149-153 (June) 1957.

Autopsy of child showed no skin lesions but a diffuse meningeal hemorrhage as well as many petechiae in the cerebellar region. The child died at birth.

DERBES, New Orleans.

IMPORTANCE OF PATCH TESTS WITH ACID AND ALKALI FOR ECZEMA DIAGNOSIS. A. W. ENGLEHARDT, H-J. HEITE and H. P. JACKEN, Arch. klin. u. exper. Dermat. 207:323-338 1958.

In 53 normal persons and 145 persons suffering from various dermatoses among which eczema is included, patch tests with a test plaster (Beiersdorf), containing 116 mg. of NaOH resp. HCl solution in dosages varying from 0.32% to 6.3% NaOH and from 0.29 to 5.77% HCl, were performed. Erythema resp. beginning necrosis determined the threshold of irritation for HCl resp. NaOH. There was significant difference of the HCl erythema threshold between eczematous and normal persons. NaOH tests showed sensitivity increase in neurodermatitis only. Patch tests with HCl and NaOH are not specific and of very little importance. Anamnestic findings about increased sensitivity to wool, soap, and adhesive tape are of certain value.

HOLLANDER, Springfield, Mass.

DISTURBANCES OF PERIPHERAL BLOOD CIRCULATION BY MEASUREMENT OF SKIN TEMPERATURE. W. SCHULZE and H. H. SCHULDT, Arch. klin. u. exper. Dermat. 207:541-553, 1958.

Description of a method for the examination of accelerating and inhibiting influences on the blood circulation of digital vessels. This method combines Burckhardt's rewarming test and W. Schulze's permanent cooling test.

HOLLANDER, Springfield, Mass.

CUTANEOUS FORM OF HEPATIC PORPHYRIA AND PORPHYRINURIA. G. LEONHARDI and M. BAIER, Arch. klin. u. exper. Dermat. 207:554-575, 1958.

Analysis of urinary porphyrins and their isomers by quantitative determinations and paper chromatography in eight patients with cutaneous form of hepatic porphyria showed increased excretion of uroporphyrin in the urine in all cases; coproporphyrin amounts were partly increased, and traces of proto- and deuteroporphyrins were found. Uroporphyrin and coproporphyrin isomers of Type I prevailed. In the cutaneous form of hepatic porphyria the liver cannot sufficiently decarboxylate and dehydrate uroporphyrin to protoporphyrin. The synthesis of hemin in the liver remains on the level of uroporphyrin. Therapeutic attempts with liver hydrolysates and vitamin B failed in one patient; prednisone decreased urinary excretion of porphyrin for a while.

HOLLANDER, Springfield, Mass.

PROBLEMS AND RESULTS OF X-RAY STUDIES OF THE SKIN AND ITS DISEASES: PT. 2. X-RAY FINDINGS IN PATHOLOGIC SKIN. G. LEMKE, Arch. klin. u. Dermat. 207:576-616, 1958.

Numerous dermatoses including common dermatoses, such as dermatitis, eczema, psoriasis, and urticaria, were examined by soft x-ray technique. Some dermatoses showed changes of the cutis line and the finer subcutaneous structure. Demonstration of subcutaneous and perivascular infiltrates was possible. In a few cases smaller vessels with thickened walls could be seen on the border of cutis and subcutis. A number of dermatoses revealed characteristic findings. Author believes that the term "special dermatologic x-ray diagnosis" can already be used.

HOLLANDER, Springfield, Mass.

EXPERIMENTAL DATA CONCERNING THE FUNCTION OF THE WATER BARRIER IN THE LIVING HUMAN EPIDERMIS. A. SZAKALL, Berufsdermatosen 6:171-192 (Aug.) 1958.

The osmotic behavior of the lower stratum corneum (conjunctum) in its normal and defatted state is studied in its relation to the stratum granulosum as well as to the superficial stratum corneum (disjunctum). The findings demonstrate and explain the function of the skin as a water barrier.

BULEY, Champaign, Ill.

PRE-EMPLOYMENT DERMATOLOGICAL EXAMINATIONS AS PROPHYLAXIS AGAINST OCCUPATIONAL DERMATOSES. H. WEITGASSER, Berufsdermatosen 6:192-199 (Aug.) 1958.

Preemployment testing, in occupations in which the occurrence of eczematous dermatitis is common, may substantially reduce the morbidity rate of such dermatoses.

BULEY, Champaign, Ill.

SUN PROTECTION BY ESTERS AND AMIDES OF p-METHOXY-CINNAMIC ACID, STUDIED DURING ACTUAL EXPOSURE IN THE ENGADIN. W. SCHNEIDER and H. TONNIER, Berufsdermatosen 6:199-206 (Aug.) 1958.

Patent preparations containing *p*-methoxy-cinnamic acid provided a high degree of protection against ultraviolet rays, as demonstrated by exposure tests to an artificial ultraviolet source as well as to actual sun light in the Engadin, an Alpine valley. It is pointed out, however, that the protective effect varies with the type of vehicle used in the preparations.

BULEY, Champaign, Ill.

CUTANEOUS CHANGES FOLLOWING OCCUPATIONAL CONTACT WITH ETHYLENE OXIDE. P. D. BLANDIN, Berufsdermatosen 6:217-222 (Aug.) 1958.

Ethylene oxide, frequently used in pest control, may elicit symptoms of general poisoning as well as severe acute dermatitis. Two cases of this kind are reported.

BULEY, Champaign, Ill.

WETTING, SPREADING, AND CREEPING OF FATS AND OILS ON THE SKIN. O. JACOBI, Berufsdermatosen 6:241-250 (Oct.) 1958.

A method of determining the spread of different fats and oils on the human skin is described. In addition to the viscosity and surface tension of the materials, the water and sebum content of the skin, and the presence of a surface-active X-substance, the main factor responsible for the spreading of the fats is the capillarity of the intercellular spaces in the superficial stratum corneum.

BULEY, Champaign, Ill.

RUBBER AND ECZEMA. E. SCHULTHEISS, Berufsdermatosen 6:267-286 (Oct.) 1958.

Completing his previous review (*Berufsdermatosen* 6:206-217 [Aug.] 1958) of eczema due to contact with rubber, the author gives a detailed monographic review of the technological aspects of rubber production insofar as it is of interest to the industrial physician and especially the industrial dermatologist.

BULEY, Champaign, Ill.

THE PATHOLOGICAL EFFECTS OF SMALL DOSE OF RADIATION. S. WARREN, Bull. New York Acad. Med. 34:633-640 (Oct.) 1958.

Survivors of the atomic bombing in Japan indicate three important effects: 1. A single dose of radiation may produce leukemia. 2. Only a small part of the heavily exposed population (less than 2%) will develop leukemia. 3. There is an increased incidence of leukemia between 5 and 10 years after a single whole-body exposure. The author speculates the threshold for the induction of leukemia to lie between 50 and 100 r, lower in infants. It has been estimated from experimental and clinical data that the life-span shortening may be 1.1 days per roentgen. This hazard is rapidly being eliminated by present standards of protection, which reduce the exposure risks to acceptable levels. Radiologists, as a group, die five years earlier than the corresponding male population over 25 years of age, but this life shortening is not due to leukemia or skin cancer but rather to a nonspecific effect that might be characterized as premature aging.

BLANK, Miami, Fla.

SUPERFICIAL RADIATION THERAPY OF LARGE SKIN AREAS. R. BRAAMS, Dermatologica 117:204, 1958.

Attention is drawn to the relatively large doses of x-rays which are delivered to the total body in the case of treatment of extensive skin lesions. Shielding of each individual lesion greatly reduces the total dose which is finally delivered to the body. Different treatment methods, employing x-rays or electrons from high voltage generators and radioactive isotopes, are compared.

MONASH, Miami, Fla.

COMPARATIVE STATISTICAL INVESTIGATIONS ON THE EFFECT OF THE HARDNESS OF X-RAYS AND THE DOSAGE SIZE ON THE RESULTS OF X-RAY TREATMENT OF ECZEMA. R. H. BROWN, Dermatologica 117:215, 1958.

Lower doses (60 r) and weak radiation (tube with beryllium window, 30 kv., 0.5 mm. Al, and tubes with 0.3 mm. glass walls, 70 kv., without filter) gave considerably better results than higher doses (100 r) and stronger radiation (tube with glass wall, 100 kv., and 1-2 mm. Al).

MONASH, Miami, Fla.

EARLY DETECTION OF MELANOBLASTOMAS. N. MELCZER and J. KISS, Dermatologica 117:242, 1958.

The authors had previously described an electrometric method for the early detection of cancerous growths of the skin (*Nature, London* 179:117, 1957). It is based on the lowering of potential resistance over the cancerous area. In 465 persons with pigmented nevi and 23 with juvenile melanoma, the authors had negative results, but with 14 cases of malignant melanoma, 2 of which were achromic, they always obtained positive values. In one of four cases of melanotic precancerous freckle, in which a lowering of resistance suggested the beginning of a malignant change, histological examination revealed malignant change.

MONASH, Miami, Fla.

TROPHIC LESIONS OF THE SKIN FOLLOWING OPERATIVE PROCEDURES ON THE TRIGEMINAL NERVE (ELECTROCOAGULATION OF THE GASSERIAN GANGLION). ARTHUR LEINBROOK, Hautarzt 9:346-350 (Aug.) 1958.

The author reports his observations of rare trophic changes which may occur on the scalp and face after electrocoagulation of the gasserian ganglion in the treatment of trigeminal neuralgia.

BULEY, Champaign, Ill.

THE ETIOLOGY AND PATHOGENESIS OF PSORIASIS VULGARIS. N. MELCZER and J. BODZAY, Hautarzt 9:351-355 (Aug.) 1958.

The plaque of psoriasis is the result of an accumulation of lipids, probably lecithin, which, in turn, effects the liberation of histamine-like substances. This thesis is based on histochemical

observations and experimental intracutaneous injections of lipids into the skin of psoriatics and control subjects.

BULEY, Champaign, Ill.

THE PROBLEM OF TRANSITIONAL FORMS BETWEEN RETICULOSIS AND RETICULUM-CELL SARCOMA. A. MUSGER, Hautarzt 9:355-360 (Aug.) 1958.

The author's observations of a recent case demonstrate the transition from reticulosis to reticulum-cell sarcoma. The difference between destructive growth and malignancy is defined, and it is pointed out that destructive growth alone is not sufficient to designate a tumor as being malignant.

BULEY, Champaign, Ill.

REACTIONS OF THE CUTANEOUS VEGETATIVE NERVES TO ROENTGEN RAYS AND OTHER NOXAE. A. MIDANA and F. ORMEA, Hautarzt 9:360-362 (Aug.) 1958.

Experiments on human skin show that roentgen rays, not unlike other irritants, are capable of producing proliferative as well as degenerative changes in the vegetative nerves, the type of alteration depending on the doses of radiation administered.

BULEY, Champaign, Ill.

NODULAR APHTHOSIS, APHTHOSIS "EN PLAQUES" AND PFEIFFER-WEBER-CHRISTIAN PANNICULITIS. X. VILANOVA and J. P. AGUADÉ, Hautarzt 9:389-398 (Sept.) 1958.

In six cases of nodular vasculitis, the lesions are assumed to be etiologically related to aphthosis (Behçet's syndrome). Intracutaneous injections of an antigen obtained from saliva produced clinical and histological changes identical with those of nodular vasculitis.

BULEY, Champaign, Ill.

SYMPTOMATOLOGY AND DIFFERENTIAL DIAGNOSIS OF "ERYTHEMATOSUS-LIKE LIGHT DERMATOSIS." G. WEBER, Hautarzt 9:400-406 (Sept.) 1958.

"Erythematosus-like light dermatosis," as a clinical entity, is distinguished from chronic erythematosus and chronic polymorphous light eruption. A report of four cases serves to illustrate the author's thesis.

BULEY, Champaign, Ill.

THE PATHOGENESIS OF THE NUCHAL NEVUS (UNNA) AND THE TELANGIECTATIC NEVUS OF THE FOREHEAD. W. BLAICH, Hautarzt 9:406-409 (Sept.) 1958.

The telangiectatic nevi of forehead and nape of neck are attributed to nerve damage caused by trauma during birth.

BULEY, Champaign, Ill.

ROENTGEN RAY DIFFRACTION STUDIES IN SCLERODERMA DIFFUSA AND CIRCUMSCRIPTA. E. MACHER and B. BREHLER, Hautarzt 9:409-414 (Sept.) 1958.

In four cases of diffuse progressive scleroderma and in five cases of the circumscribed form of the disease, the molecular structure of the collagenous fibers was examined by means of the Debye-Scherrer technique of x-ray diffraction. A quantitative deviation from the norm, found in four cases of circumscribed scleroderma, is apparently caused by the loss of the amorphous interstitial substance separating the crystalline fiber elements.

BULEY, Champaign, Ill.

SELF-DEPRESSION OF THE SUBCUTANEOUS ABSORPTION OF DRUGS DUE TO RELEASE OF HISTAMINE. JENS SCHOU, Nature, London 182:324 (Aug. 2) 1958.

In rabbits and rats there is reduced absorption for the first 20 minutes after injection subcutaneously of an aqueous solution of sodium sulfacetamide. This is attributed to histamine liberated from mast cells by the trauma of injection. Treatment with an antihistamine drug, mepyramine maleate, or depletion of histamine with compound 48/80 prevents the reduced absorption.

MONASH, Miami, Fla.

RADIOACTIVE WRIST WATCHES. G. D. CHASE and A. OSOL, Science 128:788 (Oct.) 1958.

The degree of radioactivity of 20 luminous-dial wrist watches was found to vary from 1 mr per hour to 10 mr per hour at a distance of 1 in. from the face of the watch. At a distance of 8 in. the most active watches could deliver 1.1 r a year to the gonads if worn

24 hours a day, or a potentially harmful magnitude of 5 rem in about five years. This is a potential hazard when judged by the recommendation of the International Commission on Radiation Protection that no one should receive a dose in excess of 5 rem by the age of 30 years.

BLANK, Miami, Fla.

ULTRAVIOLET MITIGATION OF X-RAY LETHALITY IN DIVIDING YEAST CELLS. M. M. ELKIND and H SUTTON, Science 128:1082-1083 (Oct. 31) 1958.

The lethal effect of x-rays on dividing yeast cells can be decreased by small ultraviolet exposures delivered before or after x-ray exposure. This mitigating action can be decreased by exposure to visible light concomitant with photoreactivation of ultraviolet lethality. The results suggest considerable overlap between x-ray and ultraviolet lethality sites in dividing cells.

BLANK, Miami, Fla.

OROPHARYNGEAL HISTOPLASMOSIS TREATED WITH DIAMIDINODIPHENYLAMINE. J. E. MACKINNON and V. STAPFF, Tr. Roy. Soc. Trop. Med. & Hyg. 52:290, 1958.

The authors report a patient with an extensive ulcerous, granulomatous, and vegetating lesion of the mucosa with pulmonary lesions. In confirmation of their in vitro studies with Diamidinodiphenylamine, which was highly active against Histoplasma capsulatum as well as Paracoccidioides brasiliensis, administration intravenously in two courses produced healing and apparent recovery of the patient.

BLANK, Miami, Fla.

CHANGES IN NUCLEIC ACID CONTENT OF HELA CELLS INFECTED WITH HERPES VIRUS. A. NEWTON and M. G. P. STOKER, Virology 5:549-560 (June) 1958.

The nucleic acid content of HeLa-type tissue culture cells was increased after injection with herpes simplex virus. The deoxyribonucleic acid (DNA) nearly doubled, but there was no significant change in ribonucleic acid (RNA) content. This preceded and paralleled increase in infective virus, confirming again that virus multiplies in the nucleus in this infection.

BLANK, Miami, Fla.

PROPERDIN SENSITIVITY OF HERPES SIMPLEX VIRUS (Letter to the editor). R. A. FINKELSTEIN, R. ALLEN and S. E. SULKIN, Virology 5:567-568 (June) 1958.

The authors found that a heat-labile component of normal rat serum had an inhibitory effect on herpes simplex virus when tested in HeLa tissue culture cells. The factor seems to be identical with properdin and purified human properdin was demonstrated also to have inhibitory effect. The authors speculate that variations in the properdin levels which can be produced by stimuli, such as fever, fatigue, and other stresses, may be the mechanism in the appearance of recurrent herpetic lesions in man.

BLANK, Miami, Fla.

INTRANUCLEAR CRYSTALS OF HERPES SIMPLEX VIRUS OBSERVED WITH THE ELECTRON MICROSCOPE (Letter to the editor). C. MORGAN, E. P. JONES, M. HOLDEN, and H. M. ROSE, Virology 5:568-571 (June) 1958.

In excellent electron micrographs the authors have demonstrated additional details in their continuing study of herpes simplex within the nucleus of infected cells. They now demonstrate that the cell nuclei contain herpes simplex virus arranged in a crystalline lattice. This has been demonstrated in the past for a wart virus and a few other viruses. In addition to the ordered array of the virus, the fine structure of the virus particles is further revealed to consist of a dense internal body, approximately 40 mμ in diameter, surrounded by a single, sharply defined membrane, about 90 mμ in diameter. Extracellular viral particles have a double limiting membrane in distinction to the intranuclear virus.

BLANK, Miami, Fla.

ISOLATION OF HERPES ZOSTER VIRUS FROM SPINAL FLUID OF A PATIENT (Letter to the editor). E. GOLD and F. C. ROBBINS, Virology 6:293-295 (Aug.) 1958.

The authors cultured the virus of zoster and varicella in tissue cultures of human amnion or monkey kidney cells from vesicle fluids. Typical cytopathic effects in the cells were noted with the appearance of intranuclear inclusions.

Antigen for complement-fixation tests has been prepared from the agents of varicella and herpes zoster. These agents cannot be differentiated by complement-fixation techniques; convalescent sera from patients with herpes zoster give a positive reaction with either herpes zoster or varicella antigen and vice versa.

Studies with the complement-fixation test have shown the uniform acquisition of antibody by all patients with varicella. Of five patients with herpes zoster who have been studied, two showed a fourfold or greater rise in antibody during their illness but three had high levels of antibody in their initial serum specimens with no significant increase in the convalescent specimen.

The authors report the isolation of a cytopathogenic agent, which they felt was the virus of zoster, from the spinal fluid of a 6½-year-old child. This is believed to be the first report of the isolation of this agent from spinal fluid.

BLANK, Miami, Fla.

THE FORMATION OF MICROSCOPIC PLAQUES BY HERPES SIMPLEX VIRUS IN HELA CELLS. A. E. FARNHAM, Virology 6:317-327 (Oct.) 1958.

In the absence of an agar overlay or herpes antiserum microscopic plaques form in HeLa cell cultures as a result of infection with herpes virus. Strict proportionality between plaque numbers and the virus input exists. The efficiency of plaque formation was influenced by the inoculum size and the adsorption period. The relative sensitivity of HeLa cells for herpes virus titrations was discussed.

BLANK, Miami, Fla.

CORRECTION

In the March issue of the ARCHIVES, page 54/**264**, the first sentence of the first paragraph in the second column should read:

"Direct bioassay of the urine from six patients indicated excretion by this route of more than 50% of orally administered griseofulvin."

Announcements

First Canadian Symposium on Non-Gonococcal Urethritis and Human Trichomoniasis. On Sept. 21 and 22, 1959, at Notre-Dame Hospital in Montreal, under the patronage of the Honorable Waldo J. Monteith, Minister of National Health and Welfare, and of the Honorable Arthur Leclerc, M.D., Minister of Health of the Province of Quebec, will be held the First Canadian Symposium on Non-Gonococcal Urethritis and Human Trichomoniasis.

For all information, write to Secretary of the Symposium, 8580 Esplanade Ave., Montreal 11.

Scientific Exhibits.—Applications are now being received for space for scientific exhibits at the meeting of the American Academy of Dermatology at the Palmer House, Chicago, in December, 1959.

Awards will be given for the best exhibits in each of the following categories: (1) original investigation, (2) teaching value, and (3) historical.

Please address all correspondence before the application deadline, June 1, 1959, to Frederick D. Malkinson, M.D., Section of Dermatology, University of Chicago Clinics, 950 E. 59th St. Chicago (37).

Continuation Course in Allergy.—A continuation course in allergy for general physicians and specialists will be presented by the University of Minnesota on April 16 to 18, 1959, at the Center for Continuation Study. The general principles of diagnosis and treatment of clinical allergy will be stressed.

Guest speakers will be Drs. Mary H. Loveless, New York Hospital, New York, and Herbert J. Rinkel, Kansas City, Mo. The course will be presented under the direction of Dr. J. S. Blumenthal, Clinical Associate Professor of Medicine, and the remainder of the faculty will be drawn from the faculties of the University of Minnesota Medical School and the Mayo Foundation.

Lodging and meal accommodations are available at the Center for Continuation Study.

Books

The Birth of Normal Babies. By Lyon P. Strean, Ph.D., D.D.S., F.A.P.H.A. Foreword by H. E. Lehmann, M.D. Price, $3.95. Pp. 194. Twayne Publishers, Inc., 31 Union Sq., New York 3, 1958.

The thesis presented here is that the major cause of defective babies can be attributed to the occurrence of stress in the first trimester of pregnancy. The stress may result from a drug reaction, infectious disease, physical trauma, metabolic disease, or emotional upheaval—anything that affects the adrenals. Case examples are cited: A pregnant woman with five normal children was treated for generalized psoriasis with corticosteroids. The sixth infant had a cleft palate. Cases of mental deficiency, miscarriages, malformations are attributed to drug reactions, poison ivy, pemphigus, etc., all on *post hoc, propter hoc* reasoning. The writing is very simple, not even of the order of a good newspaper health column. The book is intended for lay persons—to teach them how to avoid abnormal birth results.

Essentials of Therapeutic Nutrition. By Solomon Garb, M.D. Price, $2. Pp. 147. Springer Publishing Company, Inc., 44 E. 23d St., New York 10, 1958.

Dr. Garb, a pharmacologist, has written a brief, informative book that is "patient-centered" rather than "food-centered." It contains a section on the principles of nutrition, another on therapeutic diets of all sorts, and one of quick reference tables of the composition of foods. It is a fine reference for nurses and students or for anyone lecturing to such groups.

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1957

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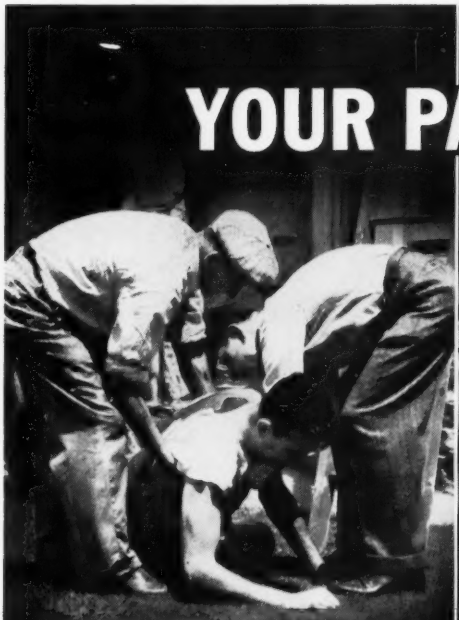

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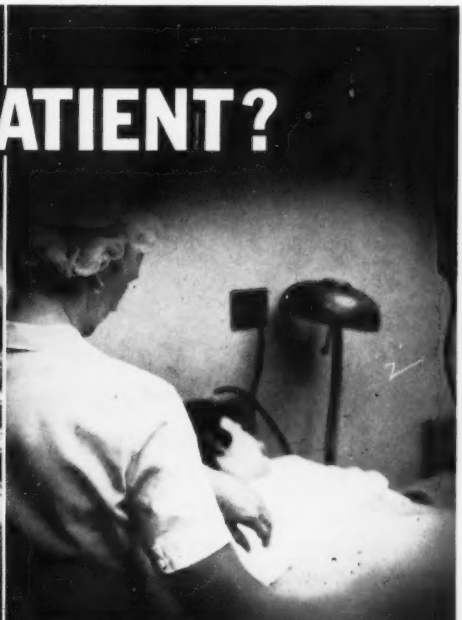

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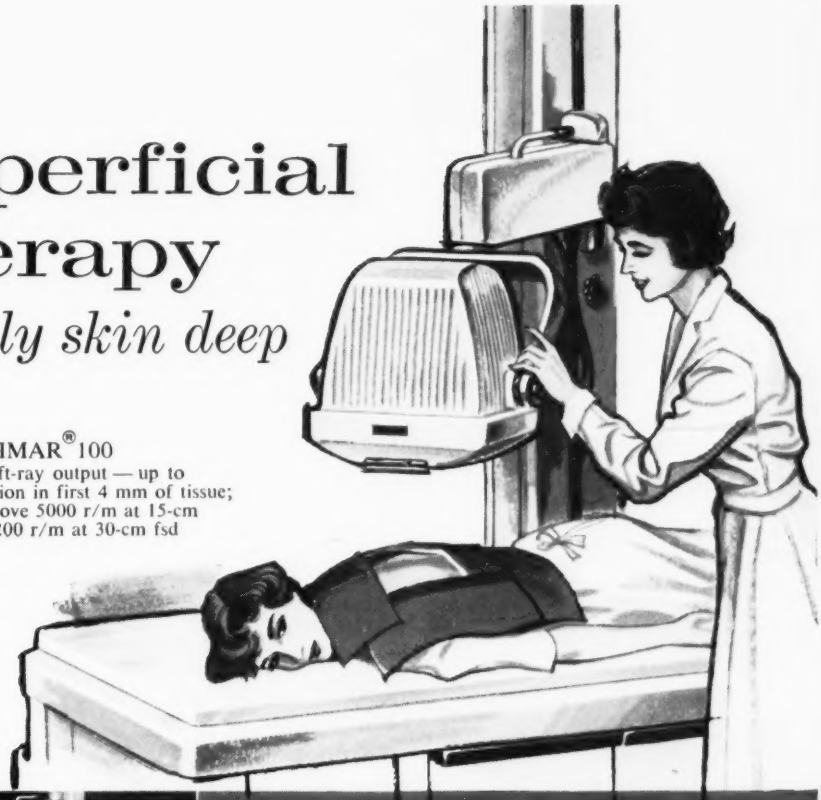

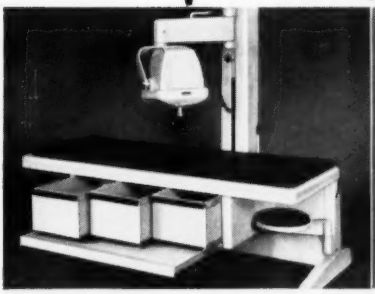

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REFERENCES: 1. R. J. Schnitzer, E. Grunberg, W. F. DeLorenzo and R. E. Bagdon, to be published.
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3. R. C. V. Robinson and L. E. Harmon, **Antibiotics Annual 1958-1959.**

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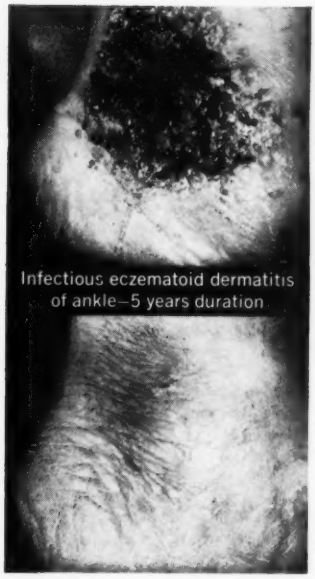

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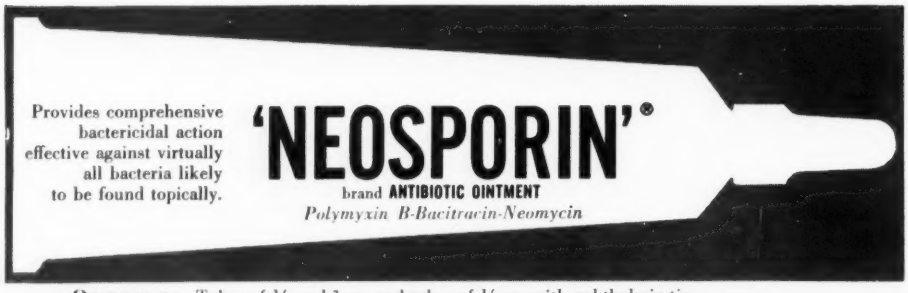
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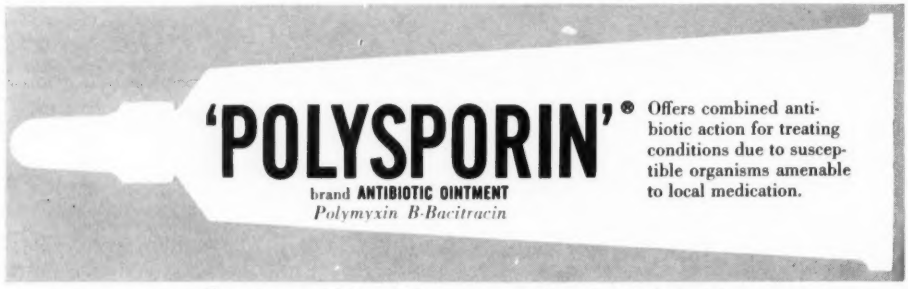
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Texas J. Med. *53*:640 (Aug.) 1957

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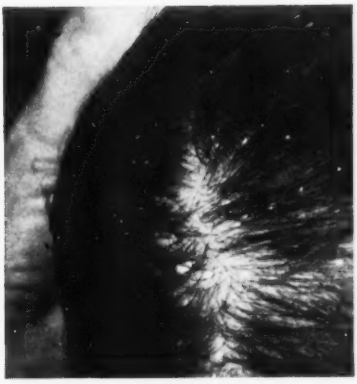

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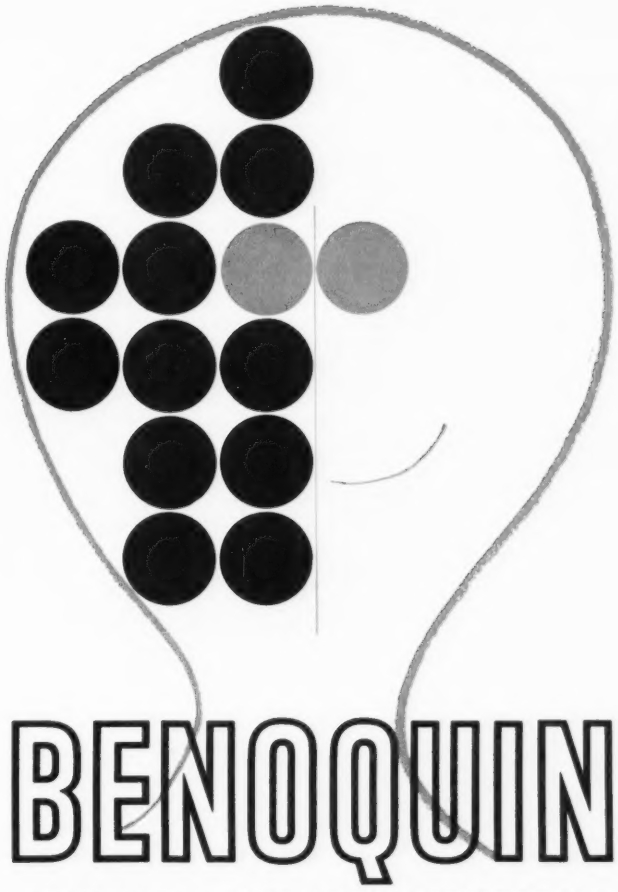

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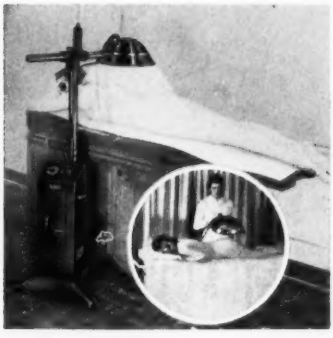

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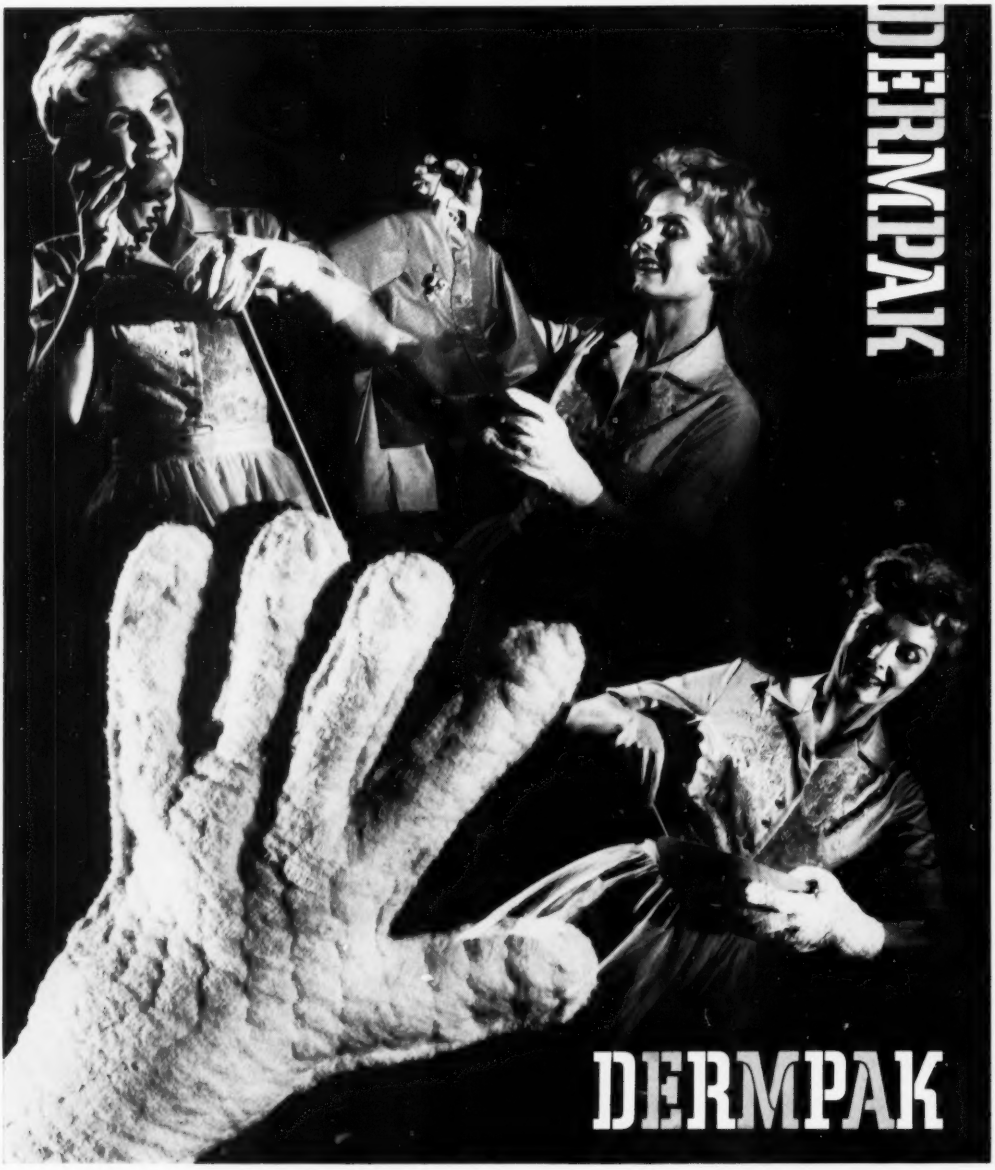

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BIBLIOGRAPHY: 1. S. Fisher, J. Med. Soc. New Jersey, 53,292-294, 1956. 2. R. Ehrlich, Am. J. Proctology, 7,497-498, 1956. 3. J. G. Downing, M. Clin. North America, 1245-1265, 1955, Saunders. 4. N. Tobias, Essentials of Dermatology, p. 599, 1956, Lippincott.

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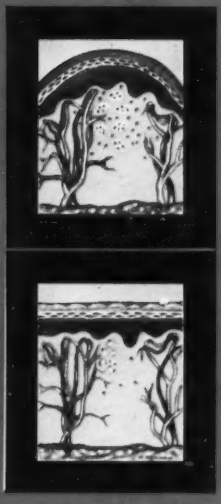

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1. Welsh, A. L., and Eds, M.: J.A.M.A. 166:154, 1958.

Additional Clinical Publications on Tarcortin:

Clyman, S. G.: Postgrad. Med. 21:309, 1957 • Bielberg, J.: J. M. Soc. New Jersey 53:37, 1956 • Abrams, B. P., and Shaw, C.: Clin. Med. 3:639, 1956 • Bielberg, J.: Am. Practitioner 8:1404, 1957

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1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

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